"CLINICAL AND LABORATORY PROFILE OF NEWLY DIAGNOSED, HIV-INFECTED PATIENTS ATTENDING ART CENTRE, TVMCH, TIRUNELVELI"

Dissertation submitted to

THE TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY

CHENNAI, TAMIL NADU

in partial fulfillment for the Degree of

DOCTOR OF MEDICINE - BRANCH I GENERAL MEDICINE

APRIL 2016

TIRUNELVELI MEDICAL COLLEGE HOSPITAL

TIRUNELVELI – 11, TAMIL NADU

CERTIFICATE

This is to certify that the Dissertation entitled **"CLINICAL AND LABORATORY PROFILE OF NEWLY DIAGNOSED, HIV-INFECTED PATIENTS ATTENDING ART CENTRE, TVMCH, TIRUNELVELI"** submitted by **Dr.ALGIN DANNY.A** to The Tamilnadu Dr. M.G.R. Medical University, Chennai, in partial fulfillment for the award of M.D.Degree(GENERAL MEDICINE) is a bonafide work carried out by him under my guidance and supervision during the course of study 2013-2016. This dissertation partially or fully has not been submitted for any other degree or diploma of this university or other.

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DECLARATION

I solemnly declare that the dissertation titled "**CLINICAL AND LABORATORY PROFILE OF NEWLY DIAGNOSED, HIV-INFECTED PATIENTS ATTENDING ART CENTRE, TVMCH, TIRUNELVELI**" is prepared by me.

The dissertation is submitted to The Tamilnadu Dr,M.G.R.Medical university towards the partial fulfilment of requirements for the award of M.D.Degree (Branch I) in General Medicine . I also solemnly declare that this bonafide work or a part of this work was not submitted by me or any others for any award, degree, diploma to any university, found either in India or abroad.

Place: Tirunelveli.
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CERTIFICATE OF REGISTRATION & APPROVAL OF THE TIREC REF NO: 540/GM/2014/47

PROTOCOL TITLE: CLINICAL AND LABORATORY PROFILE OF NEWLY DIAGNOSED HIV INFECTED PATIENTS ATTENDING ART CENTRE, TIRUNELVELI MEDICAL COLLEGE HOSPITAL, TIRUNELVELI.

NAME OF PRINCIPAL INVESTIGATOR: Dr. Algin Danny, MBBS.,
DESIGNATION OF PRINCIPAL INVESTIGATOR: Post Graduate in MD General Medicine
DEPARTMENT & INSTITUTION: Department of General Medicine, Tirunelveli Medical College

Dear Dr. Algin Danny, *The Tirunelveli Medical College Institutional Ethics Committee (TIREC) reviewed and discussed your application during the IEC meeting held on 14.05.14.*

THE FOLLOWING DOCUMENTS WERE REVIEWED AND APPROVED

1.	TIREC Application Form	☐
2.	Study Protocol	☐
3.	Department Research Committee Approval	☐
4.	Patient Information Document and Consent Form in English and Vernacular Language	☐
5.	Investigator's Brochure	☐
6.	Proposed Methods for Patient Accrual Proposed	☐
7.	Curriculum Vitae of the Principal Investigator	☐
8.	Insurance /Compensation Policy	☐
9.	Investigator's Agreement with Sponsor	☐
10.	Investigator's Undertaking	☐
11.	DCGI/DGFT approval	☐
12.	Clinical Trial Agreement (CTA)	☐
13.	Memorandum of Understanding (MOU)/Material Transfer Agreement (MTA)	☐
14.	Clinical Trials Registry-India (CTRI) Registration	☐

THE PROTOCOL IS APPROVED IN ITS PRESENTED FORM ON THE FOLLOWING CONDITIONS

1. The approval is valid for a period of 2 year/s or duration of project whichever is later
2. The date of commencement of study should be informed
3. A written request should be submitted 3weeks before for renewal / extension of the validity
4. An annual status report should be submitted.
5. The TIREC will monitor the study
6. At the time of PI's retirement/leaving the institute, the study responsibility should be transferred to a person cleared by HOD
7. The PI should report to TIREC within 7 days of the occurrence of the SAE. If the SAE is Death, the Bioethics Cell should receive the SAE reporting form within 24 hours of the occurrence.
8. In the events of any protocol amendments, TIREC must be informed and the amendments should be highlighted in clear terms as follows:
    a. The exact alteration/amendment should be specified and indicated where the amendment occurred in the original project. (Page no. Clause no. etc.)
    b. The PI must comment how proposed amendment will affect the ongoing trial. Alteration in the budgetary status, staff requirement should be clearly indicated and the revised budget form should be submitted.
    c. If the amendments require a change in the consent form, the copy of revised Consent Form should be submitted to Ethics Committee for approval. If the amendment demands a re-look at the toxicity or side effects to patients, the same should be documented.
    d. If there are any amendments in the trial design, these must be incorporated in the protocol, and other study documents. These revised documents should be submitted for approval of the IEC, only then can they be implemented.
    e. Approval for amendment changes must be obtained prior to implementation of changes.
    f. The amendment is unlikely to be approved by the IEC unless all the above information is provided.
    g. Any deviation/violation/waiver in the protocol must be informed

STANDS APPROVED UNDER SEAL

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Registrar, TIREC
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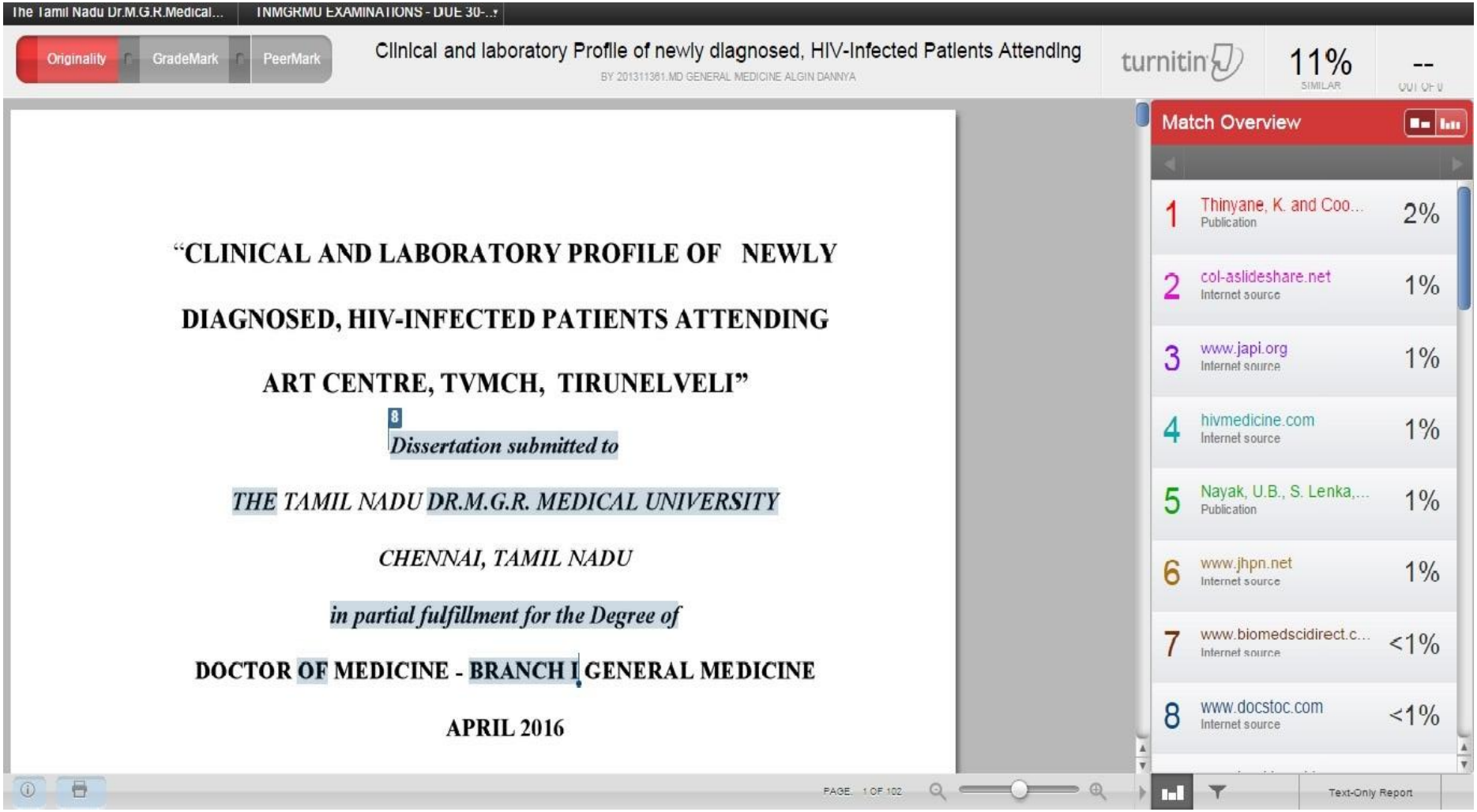
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CONTENTS

ABBREVIATIONS

AIDS - ACQUIRED IMMUNO DEFICIENCY SYNDROME

ART – ANTI RETROVIRAL THERAPY

CD4 – CLUSTER OF DIFFERENTIATION 4

CTL – CYTOTOXIC LYMPHOCYTES

HAART – HIGHLY ACTIVE ANTIRETROVIRAL THERAPY

HIV – HUMAN IMMUNO DEFICIENCY VIRUS

HSS – HIV SENTINEL SURVEILLANCE

HTLV – HUMAN T LYMPHOTROPIC VIRUS

IDU – INJECTION DRUG USERS

NACO - NATIONAL AIDS CONTROL ORGANISATION

WHO – WORLD HEALTH ORGANISATION

INTRODUCTION:

Humans have seen the emergence of many new diseases throughout the history. In the 20th century the disease which came to the fore and made the human race panic the most was Acquired Immune deficiency Syndrome (AIDS), which is caused by Human Immunodeficiency Virus (HIV). The disease surfaced in the 1980s, and three decades later, our combat with the disease is still on. Hence AIDS/HIV remains one of the most dreaded public health challenges.

Although the overall rate of new infections appears to decline, epidemics among key populations continue to grow alarmingly. This includes injection drug users (IDU), homosexuals and sex workers. Remarkable progress has been made in such populations over the last decade-yet significant challenges remain.

The absence of a cure or preventive vaccine to the disease has had its negative effect on economy and development of various developing countries like India. But a positive response from the government, NGOs and WHO have effectively brought down the transmission rates among the most vulnerable populations in India. Many studies contribute to the evidence base for emphasis on prevention as the most cost beneficial and effective national response.

EPIDEMIOLOGY OF HIV IN INDIA:

HIV Sentinel Surveillance [1] (HSS) formalised by the National AIDS Control Organisation (NACO) in India is the best source of epidemiology of HIV/AIDS in India. According to HSS 2012-2013, the overall prevalence of HIV in India continues to be as low as 0.35%. Nagaland, Mizoram, Arunachal Pradesh, Andhra Pradesh, Karnataka, Chhattisgarh, Gujarat, Maharashtra, Delhi and Punjab are the states in which the HIV prevalence was more than the national average. Bihar, Rajasthan and Odisha recorded prevalence less than the national average. The prevalence of HIV in Tamil Nadu is 0.36% which is close to the national average. Although all the states in India showed a prevalence of less than one percentage, there are certain areas within the states including Tamil Nadu which showed prevalence rate more than 1%. The estimated number of people who live with HIV in India has declined from 23.2lakhs in 2006 to 20.9lakhs in 2011.

In Tamil Nadu the prevalence rate [2] is highest among the transgender group (3.82%), Female sex workers (FSW) (2.69%) and men having sex with men (MSM) (2.4%) according to official data.

Another alarming part of HIV in India is the prevalence of Tuberculosis and HIV co-infection. A study done on the prevalence of tuberculosis in HIV positive patients attending ART centre in Maharashtra showed that about 17% of the HIV positive patients had tuberculosis co-infection.

AIM OF THE STUDY

To document,

1) The clinical profile
2) The laboratory profile
3) Clinical staging
4) Immunological staging

in 100 randomly selected newly diagnosed HIV infected patients attending ART centre , Tirunelveli medical college hospital, Tirunelveli from June 2014 to May 2015.

REVIEW OF LITERATURE

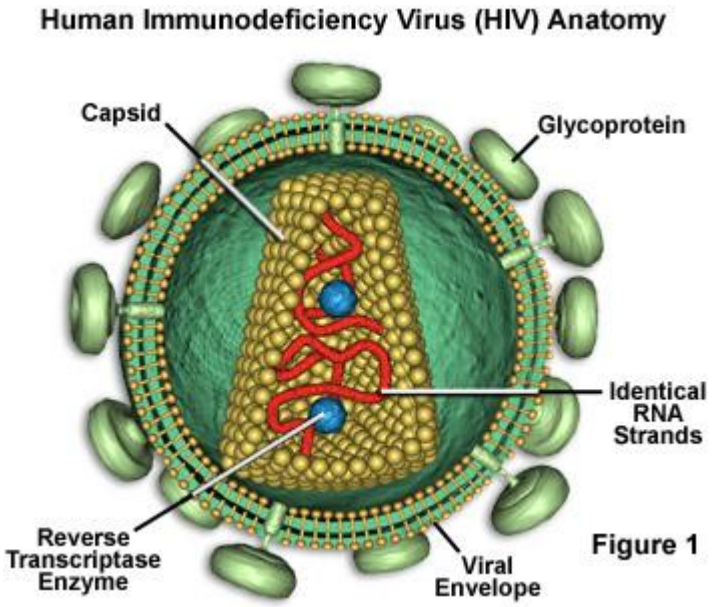


Figure 1

HUMAN IMMUNO DEFICIENCY VIRUS:

Human immunodeficiency viruses [3] belong to the family retroviridae and subfamily lentiviridae. Two types of human viruses are recognised in this subfamily HIV-1 and HIV-2. Both types of virus differ in geographical distribution, molecular and biological characteristics as well as in the manner of their transmissibility.

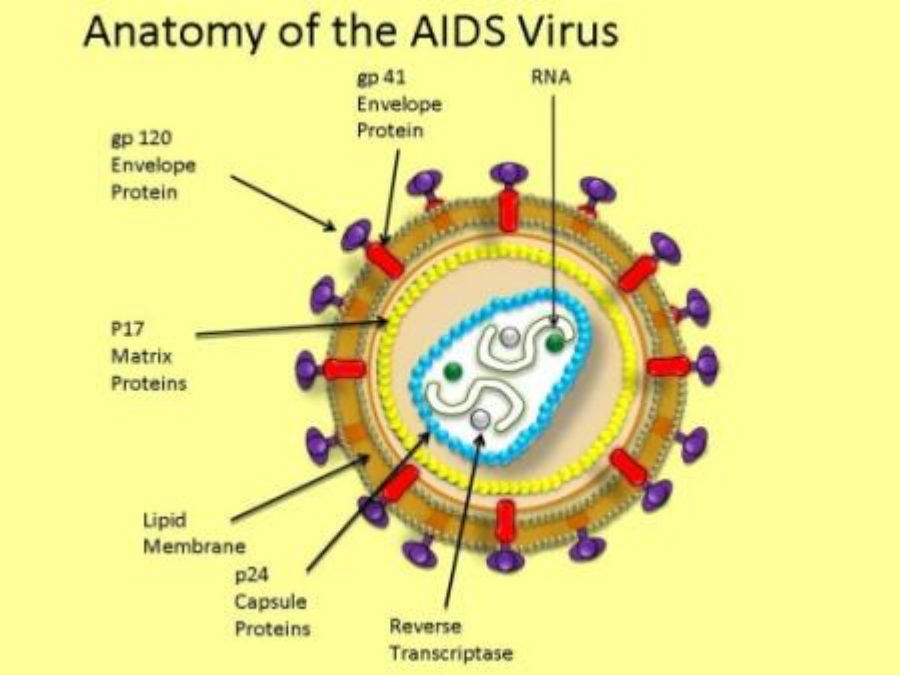
There are 3 types of HIV-1, which includes,

1) HIV-1 major group(HIV-1M)
2) HIV-1 new (HIV-1N)
3) And HIV-1 outlier(HIV-1O)

The most common cause of HIV disease all over the world and India is HIV-1. HIV-2 was identified in West Africa. It was earlier believed to be confined only to West Africa. But a number of cases which can generally be traced to West Africa or to sexual contacts with West African populations have been identified throughout the world including India. HIV-1 M group is the cause of pandemic all over the world. The human T lymphotropic viruses, HTLV-1 and HTLV-2 are other types of retroviruses that can cause diseases in humans.

MORPHOLOGY OF HIV [3]

HIV is an enveloped, positive stranded, ribonucleic acid virus. The HIV virion has an icosohedral structure containing numerous external spikes or knobs. The spikes or knobs are made of glycoproteins gp120 and gp41 in HIV-1 and gp-36 in HIV-2. The HIV virion measures 120nm in diameter. The spikes or knobs are uniformly arranged over a lipid bilayer. The two positive stranded RNA molecules are embedded in a protein capsid (p24) together with the so called viral enzymes (viral RNA dependent DNA polymerase (pol), also called as the reverse transcriptase enzyme) and nucleocapsid proteins p9 and p7. The capsid is surrounded by a matrix layer which in turn is enclosed by a lipid bilayer, called the envelope.

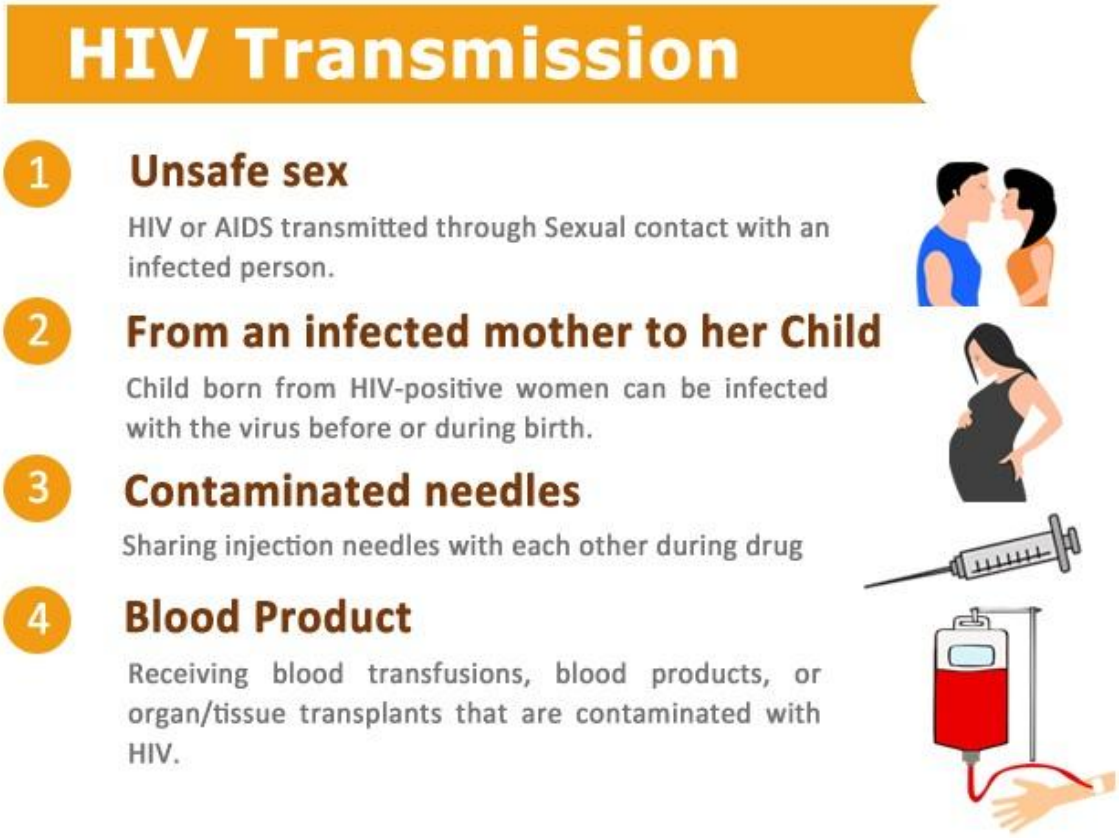


TRANSMISSION OF HIV [4]

Transmission of HIV is commonly through sexual contact which includes both heterosexual and male to male sexual contact.

It can also be transmitted through blood and blood products, and in injection drug users (IDU) through the syringes they share.

The other mode of transmission is the so called vertical transmission, which is from mother to infant, which may occur during intrapartum period, perinatal period or via breast milk.



SEXUAL TRANSMISSION:

It is the commonest mode of transmission of HIV. In the developing countries like India, heterosexual transmission is the primary mode of transmission. In western countries there is a re-emergence of male to male sexual transmission.

The presence of other sexually transmitted diseases like Treponema pallidum, Haemophilus ducreyi or Herpes simplex virus infection leads to genital ulceration and hence eases the transmission of HIV.

INJECTION DRUG USERS (IDU):

Injection drug users are exposed to HIV while sharing injection equipments such as needles and syringes, water in which they mix the drugs or the cotton which is used for filtering the drugs.

Apart from transmission during intravenous injection , subcutaneous and intramuscular injection can also transmit HIV in them.

BLOOD AND BLOOD PRODUCTS:

HIV can be transmitted to persons who receive blood transfusions or blood products from HIV infected donors. There is also evidence to support that HIV spreads through transplanted tissue. However the vast majority of HIV through this route was before 1985, after that, the transmission through blood products is on the decline due to initiation of

mandatory tests for HIV in donated blood. Eventhough testing for HIV in donated blood has become universal even in developing countries, in some countries with poor resources; HIV continues to be transmitted through blood and blood products.

Earlier , only screening for HIV – 1 in donated blood was followed, but now developed countries are also beginning to screen for HIV – 2, since HIV – 2 infection is also occurring sporadically in all parts of the world.

MOTHER TO CHILD TRANSMISSION:

HIV can be transmitted from HIV infected mother to fetus during intrapartum period, during birth or by breast feeding. The probability of HIV transmission from pregnancy till the perinatal period is about 15% to 25% in developed countries and 25% to 35% in developing countries. This difference is due to inadequate prenatal care in developing countries.

Breast feeding is an important mode of transmission in developing countries, where the mother tends to breast feed the baby for prolonged periods.

OCCUPATIONAL TRANSMISSION:

This occurs in the health care setting, mainly in the health care workers and laboratory workers. Analysis of many studies has indicated that the transmission of HIV from infected person to health care workers through needle stick injury has 0.3% chance of transmission and mucous membrane exposure has 0.09% chance of transmission, if the exposed person is not treated with anti retroviral drugs within 24 hours from the exposure time. The emergence of post exposure prophylaxis has however reduced this occupational hazard in health care workers.

HIV TRANSMISSION BY OTHER BODY FLUIDS:

Saliva of a HIV infected person contain HIV, but the transmission is negligible because, the saliva contains endogenous antiviral substances. In addition there are also glycoproteins like mucin and thrombospondin I, which prevent the transmission of HIV through saliva. Though other body fluids like tears, sweat and urine also contain HIV, there is no evidence of transmission through these body fluids. However ,for health care workers , it is important to follow universal preventive measures even when they are dealing with the above said body fluids from HIV infected individuals.

PATHOGENESIS [4]

'CD4' molecules on cells and 'gp120' molecules on HIV have affinity for each other. A chance contact leads to firm bondage and lays the foundation for cell invasion. T-helper lymphocytes (including immature, mature and derived cells), monocytes, macrophages, dendritic cells (DCs) [in epidermis (Langerhans cells), mucosal surfaces of alimentary and genital tracts, lymphoid depots and tissues], epithelial cells lining mucosae of the said tracts and microglial cells of the central nervous system (CNS) carry CD4 molecules. HIV targets them for replication.

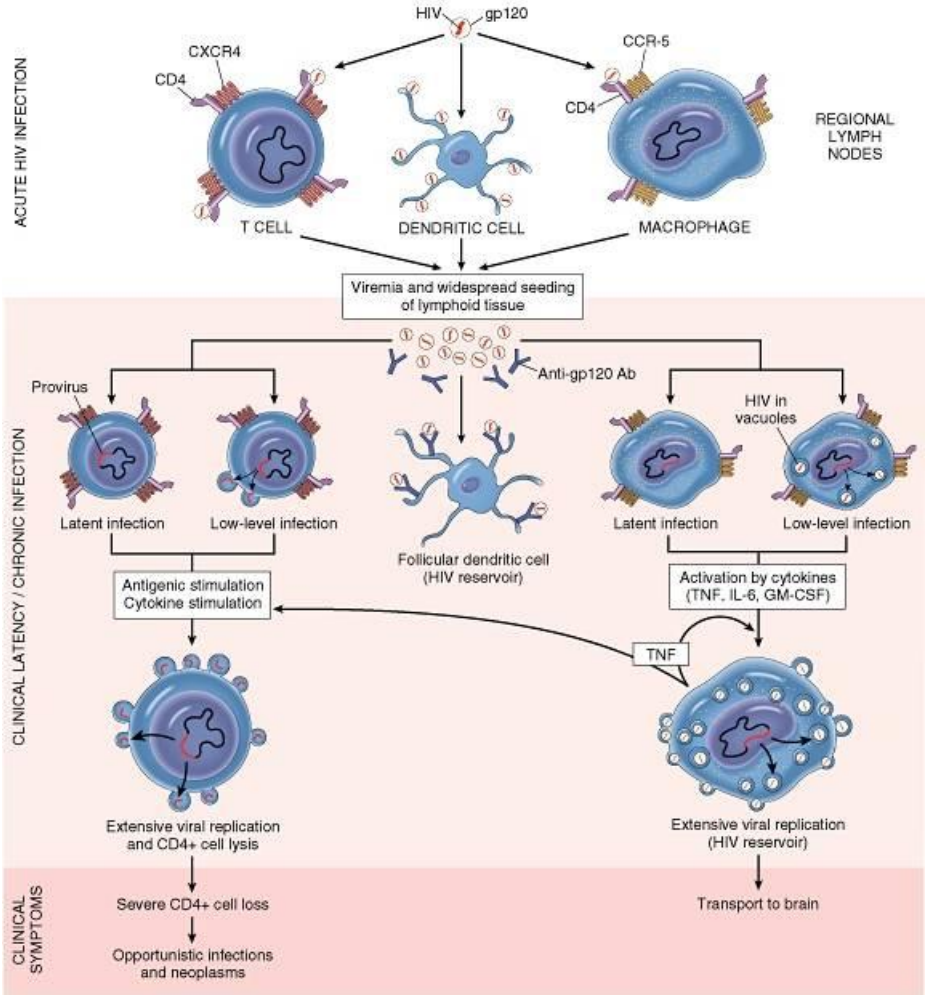
Just establishment of 'gp120↔CD4' bond does not ensure successful cell invasion, gp120 must also bind with one or more cytokines on the surfaces of target cells, which act as co-receptors. Two co-receptors, essential for HIV, are CCR5 and CXCR4. Due to minute differences in gp120 molecules, strains of HIV differ in their affinity to them. Other co-receptors (CCR2b, CCR3, STRL33 and GPR15) have also been identified. After binding with CD4, the configuration of gp120 is changed. New sites are opened on it for binding with co-receptors. After "CD4↔gp120↔CCR5/CXC4" binding, gp41 also undergoes changes. It emerges on the surface, by the side of gp120. Now, gp41 can establish contact with the target cell membrane. Molecules of 'fusion' peptides (FPs) are inserted on the exposed ends of gp41. FPs cause fusion of viral

envelope with the cell membrane. An opening is thus created. Viral genome then enters the target. This opening is sealed after viral entry. Only one virus can infect a cell. The infected cell cannot get rid of HIV.

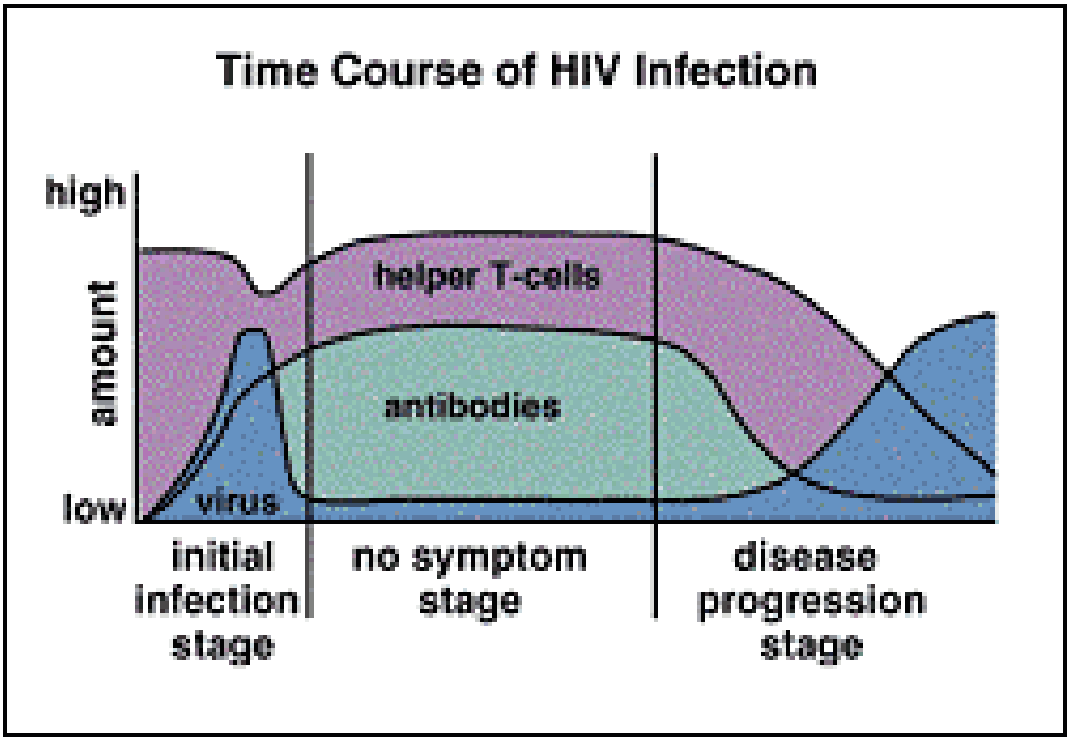
In an immunologically normal adult, immune response, as in other infections, would be expected in HIV infection too. Immune control of any viral replication is achieved through virus specific CD4+ T-cells, antibody dependent cellular toxicity and by CTLs [5]. But, in HIV infection CD4+ T-cells, themselves, are the viral targets. Due to the vagaries of HIV antigens, the magnitude and pattern of antibody response can be unreliable. Antibody levels may be high, but viral neutralisation, not proportionately so. Moreover, mutant strains can escape immune damage. CTLs are the body's major effective measure of inhibiting HIV replication. Efficiency of their action determines the future course of events. Initially, in HIV infection, they are variably successful but later on they fail. As infection continues, CTL counts fall, due to AAD(Accelerated Apoptotic Death). On exhaustion of CD8+ cells, CTL response gets suppressed (immuno suppression). Other reasons for lack of effective immune control of viral replications are magnitude of HIV reservoirs in body, functional defects in immunocompetent cells, lifestyle (intravenous drug abuse) of patient and his genetic make-up. Balance of forces 'producing and killing HIV' sets a level of viral load in body. Higher the 'set point', worse is the prognosis.

When CTL response declines, the ‘set point’ gets raised and the disease progresses faster.

PICTURE DEPICTING THE PATHOGENESIS OF HIV/AIDS



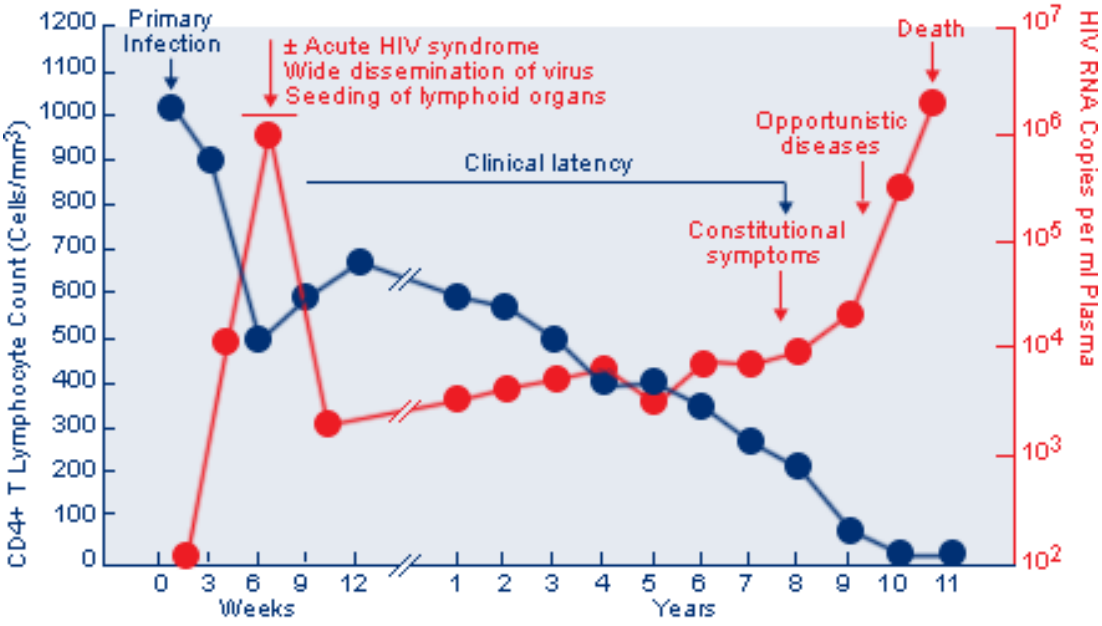
From the moment of primary infection to the development of advanced stage of the disease, there is a combination of both immunological and pathogenic events which are more complex and variable in each individual. It is also worth noting that the pathogenic mechanisms of the disease caused by HIV, involves multiple factors and is also multiphasic, hence differing at different stages of the disease [6].



CD4+ T Lymphocytes [7]

Infected cells suffer most and by various mechanisms. Even non infected cells suffer ‘accelerated apoptotic death’ (AAD), induced by excess, prolonged activation. Molecular basis of AAD is not clear. Non-infected cells, carrying viral antigens on the surface, are sequestered by anti-viral IgM/IgG antibodies and killed by cytotoxic lymphocyte (CTL) T-cells. Cells with lesser viral loads may not die but they get functionally impaired. Deficient antigen induced proliferation and cell-mediated immune (CMI) response are the major defects In active phase of infection, CD4+ loss can be up to 2 million cells per day.

GRAPH DEPICTING THE RELATION BETWEEN VIRAL LOAD AND CD4 COUNT [8]



Sometimes, loss of non-infected cells can be more than that of infected cells. In the initial phases of infection, enormous loss does not reflect as an immediate, proportionate drop in their blood count, due to compensatory proliferation of precursor cells. CD4+ counts start dropping, when the virus kills lymphoid precursor cells and replenishment of lost cells becomes increasingly inadequate [9].

PATHOGENESIS OF IMMUNODEFICIENCY

Incubation period

After transmucosal (and also parenteral) transmission, HIV reaches and establishes in T-cell areas of lymph nodes. Mucosal and nodal changes and early viral replication are clinically silent. Viral release into circulation increases slowly. Viral antigens appear in blood. HIV infection clinically manifests in 3 to 6 weeks post-exposure in up to 90% cases.

Acute retroviral syndrome (ARVS)

Increasing viraemia makes the infection manifest as ‘flu like’ episode, called ARVS (sore throat, myalgia, fever, rash, fatigue, enlarged nodes, diarrhoea and vomiting). Proportionate to the viral load in blood, there is a downward spike in CD4 count. With virus dissemination to all lymph depots, the infection becomes multi-systemic and permanent. Due to the

host's immune response, viral replication is restrained. Symptoms abate in 2 to 4 weeks. CD4 count gets corrected. Patient is sero-converted. He may be diagnosable, also by virus/its components in blood. After recovery, the patient goes through a variable period of clinical latency. Two types of 'latent' phases are possible.

Virus non-productive latent (VNPL) phase

Persons with a strong immune response take care of total viral replication while the virus lurks in reservoirs, in peaceful coexistence, awaiting an opportunity to reactivate. This can continue for months to years. The patient is sero-positive, has no viral load in blood and has a normal immune profile. Cases in VNPL phase are clinically healthy and symptom-free. They may even be noninfective to sex partners but are not safe blood donors.

Virus low-productive subdued (VLPS) phase

If the initial immune response is not strong enough to restrain viral replication completely, virus is produced in minute amount, but not sufficient to produce continuous clinical manifestations. The virus keeps on infecting new CD4+ T-cells. Its replication steadily increases without

causing a drop in their count. A period of apparent inaction continues over a variable period, depending upon the magnitude of viral replication. Patient is sero-positive. His viral load depends on the 'set point'. CD4 count, usually normal, shows a trend of gradual annual decline (25 to 60 cells per year). Cases in VLPS phase are not totally symptom-free. They may have mild/moderate episodes of symptoms due to GIT lesions. In between the episodes, they do not appear seriously ill. There may be 'non-alarming' weight loss. Their infectivity is proportional to viral load.

Persistent generalised lymph adenopathy (PGLA)

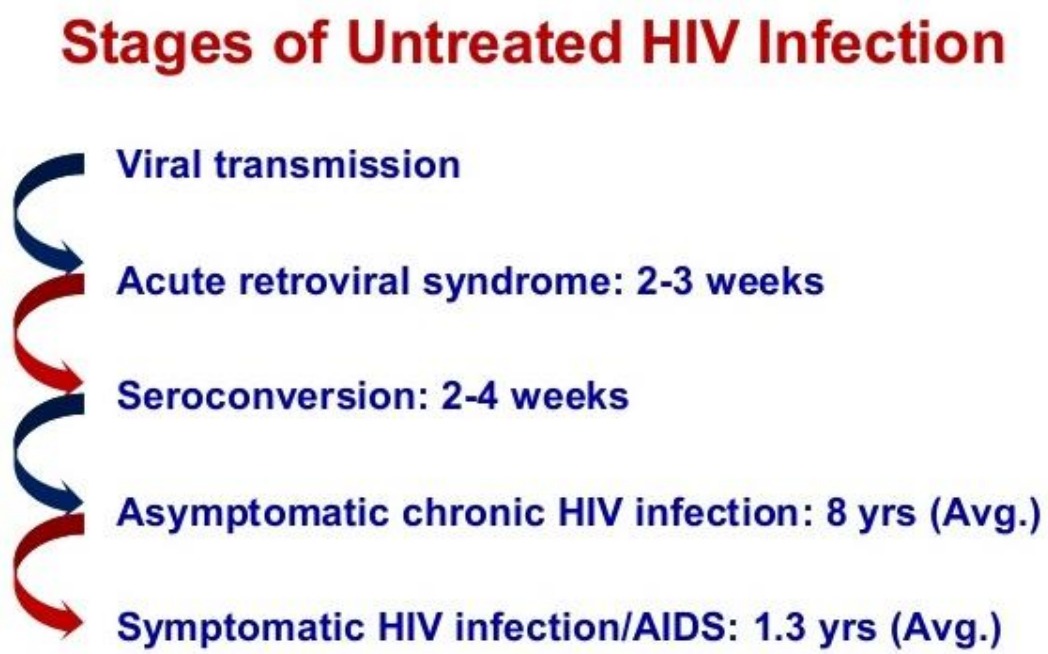
Some cases in VLPS phase have PGLA. Enlarged nodes show nonspecific polyclonal hyperplasia of 'B' and 'T' cell areas. Abnormal antibodies and their effects may appear. Some cases may have few, mild symptoms (fever, rash, fatigue). Constitutional symptoms indicate that the next stage is imminent very soon.

Stage of Immunodeficiency (SIMD) [10]

Viral replication continued over a long period, plays havoc with the immune apparatus. CD4+ T-cell plays the role of an orchestra conductor' for humoral immunity as well as CMI. Dysfunction of humoral immunity

is indirect due to influences on B-cells. Dysfunction of CMI is the direct result of loss of T lymphocytes. Progressive, relentless loss and dysfunction of almost all subsets of immunocompetent T-cells are the major events. Lymph nodes, thymus, bone marrow, lymphoid depots in tissues and gastrointestinal tract get depleted of T-cells. They show structural disorganisation and atrophy. CD4 and CD8 cell counts in blood drop. SIMD invites opportunistic pathogens and activates the pre-existing latent ones. CD4 count in peripheral blood is used as an indicator of immune function. It is however not a perfect guide. 2% of the total pool of CD4 cells is in blood and the rest is in tissues. Even a minute change in the distribution can bring about a vast change in the count. In some studies, CD4 percentage was a better marker than CD4 count. As of today, CD4 count is used and has served as a useful practical guide. Time required for progress from infection to SIMD is variable. It depends on the summation of dynamics of viral replication and the host's anti-HIV immune response. It can be prolonged by ART regime. Usually, the period cannot be predicted with certainty, except in cases in VLPS, showing decline of CD4 count at a steady rate. SIMD is reached in 2 to 5 years in 'rapid progressors'. 'Slow progressors' take more than 10 years. 8 to10 years is the period required for majority of the cases. Hallmarks of SIMD are increasing viral load, increasing titer of viral components in blood and CD4 count below 300/mL. An ill-understood group consists of patients in whom

CD4 counts are below 300/mL and yet who show no manifestations of immunodeficiency. Co-existing STD/TB viral infections accelerate the onset of SIMD. SIMD aggravates these diseases. A vicious cycle is thus established



ACQUIRED IMMUNO DEFICIENCY SYNDROME

Development of opportunistic infections (OIs) due to immunodeficiency, and/or tumours in HIV infection defines the status as AIDS. AIDS defining OIs and tumours are

- **Protozoal and Helminthic infections**
    - Cryptosporidiosis/Isosporiasis
    - Pneumocystis
    - Toxoplasmosis
- **Fungal infections**
    - Candidiasis
    - Cryptococcosis
    - Coccidioidomycosis
    - Histoplasmosis
- **Bacterial infections**
    - Atypical Mycobacteriosis
    - *Mycobacterium tuberculosis*
    - Nocardiosis
    - Salmonellosis
- **Viral infections**
    - CMV disease
    - Herpes simplex disease
    - Varicella-zoster disease

- JC polyomavirus disease

- **Tumours**
  - Kaposi's sarcoma
  - B-cell non-Hodgkin's lymphoma
  - Primary lymphoma of brain
  - Invasive cancer of cervix /Uterus

Correlation of Opportunistic infections with CD4 Lymphocyte count (/mm3)

CD4 cell count	**Infectious conditions**
>500	Candida vaginitis
200 to 500	Pneumococcal pneumonia Pulmonary tuberculosis Herpes zoster Oropharyngeal candidiasis Cryptosporidiosis Self-limited Kaposi's sarcoma Oral hairy leukoplakia
<200	*Pneumocystis jiroveci* pneumonia

	Disseminated histoplasmosis Miliary/extrapulmonary TB Progressive multifocal leucoencephalopathy
<100	Disseminated herpes simplex Toxoplasmosis Cryptococcosis Cryptosporidiosis Microsporidiosis Candida oesophagitis
<50	Disseminated cytomegalovirus (CMV) *Mycobacterium avium* complex

Opportunistic infection (OI) is a disease caused by microbial agent(s) in hosts with defects in humoral and cell mediated immunity. Immunocompromised secondary to human immunodeficiency virus (HIV) infection, use of immunomodulatory agents (including steroids and anticancer drugs) are emerging predisposing factors to OI. Opportunistic infections (OIs) may serve as indicators of underlying HIV infection. Mortality among HIV-infected individuals is due to improper awareness and consequent poor clinical management of opportunistic infections. HIV load increases in the presence of ongoing Opportunistic infections, thus accelerating progression to clinical acquired immunodeficiency syndrome (AIDS).

Changes in the CD4 lymphocyte count occur with the institution of highly active antiretroviral therapy (HAART) which in turn results in changes in OI epidemiology, clinical presentation and treatment outcomes. As HAART results in reconstitution of the immune system – certain opportunistic infections respond to HAART alone. However, the ensuing immune mediated inflammatory response may present as a paradoxical worsening of disease. It is, therefore, essential to be able to recognise and treat opportunistic infections prior to the institution of antiretroviral agents. Opportunistic infections play a role in the clinical staging of HIV infection. Opportunistic infections may present as indolent chronic infections

(pyrexia of unknown origin), reactivation of latent infections, or as acute medical emergencies. They may affect single or multiple organ systems.

Pathogenesis of GIT Lesions [11]

It is claimed (but not unanimously accepted) that GIT houses 40% to 65% of total immune cells of the body. Immune cells of GIT (all subsets of T-cells, B-cells and plasma cells, DCs and antigen identifying and processing clusters of T-cells and DCs) are organised into Peyer's patches and lymphoid follicles. They are also scattered in the lamina propria and in between the lining epithelial cells. Specialised (micro-folded) epithelial cells also act as 'immune cells'; they can take-up and transfer antigens and some pathogens to DCs. Epithelial cells bear CD4 receptors and possess the capacity to synthesise viral components and cytokines. Histology of gut mucosa is similar to that of a tissue harbouring low grade inflammation. It reflects ongoing contact and conflict with intestinal flora.

Mucosal T-memory cells are perpetually in a state of activation. Mucosal CD4+ cells are both CCR5+ and CXCR4+. They constitute 80% of the co-receptor positive population of the total body. For these reasons, the GIT is highly susceptible to HIV.

Studies on Macaque monkeys and simian immunodeficiency virus (SIV) have shown that the kinetics of destruction of immune cells of GIT was same as in other parts of the body.

Depletion of intestinal CD4+ cells was noticeable within days after infection. It was same, regardless of route of the infection. It continued throughout the course of the infection. By the time SIMD was reached, the mucosa, almost totally depleted of immunocompetent cells, was markedly thinned out. There was also direct HIV driven mucosal inflammation, a lesion called 'HIV enteropathy'.

Intestinal disease manifests with episodic diarrhoea, dehydration and anorexia. All patients do not exhibit these manifestations. When present, they may not be proportionate to the severity of the lesions. Other factors, contributory to GIT dysfunction include: fat malabsorption, bacterial overgrowth, bile salt excess and reaction to drugs. The patient is markedly emaciated.

Pathogenesis of CNS Lesions [12]

This is the third primary feature of HIV disease, even when HIV cannot cross the blood-brain barrier (BBB) and target neurones. Infected monocytes carry HIV across the BBB. A pre-existing inflammatory focus

in brain attracts HIV infested macrophages and facilitates CNS infection. M tropic strain is the main invader. CNS macrophages and microglial cells pickup HIV and suffer. About 10% of patients have short meningitic episodes at seroconversion. Serious disorder, 'dementia' (insidious onset, progressive course, impaired memory and concentration, apathy, social withdrawal, slow movements, ataxia, etc.) is seen late, when patients are approaching SIMD. Incidence (80% to 90%, prior to ART) is now declining. Virus and antibodies are present in cerebrospinal fluid (CSF). Damage is indirect, probably caused by soluble neurotoxic components (gp41 and gp120) of virus and toxic chemicals produced by infected microglia. Excess entry of calcium ions into neurones, triggered by toxic chemicals, is the postulated mechanism. The lesion is slowly destructive (focal glial necrosis) accompanied by reparative gliosis. The brain shows cerebral atrophy, widening of sulci and ventricles, microglial nodules, perivascular infiltrates and giant cell encephalitis. Clinical severity is out of proportion to the magnitude and extent of lesions. The major factor responsible for functional loss of brain is invisible: 'synaptodendritic injury (chemical injury that disrupts neuronal network function)'.

MANIFESTATIONS OF AIDS OTHER THAN OPPORTUNISTIC INFECTIONS:

CARDIOVASCULAR MANIFESTATIONS

Prevalence of cardiac involvement in HIV disease varies from 5% to 50% but symptomatic involvement occurs in 5% to 7% of patients only. Most common clinically significant cardiac abnormality due to direct HIV infection is HIV-associated dilated cardiomyopathy. There is evidence of myocarditis and HIV has been isolated from myocardial cells. Diagnosis can be supported by chest radiograph and electrocardiogram and confirmed by echocardiography and elevated serum NTproBNP. CD4+ count in these patients is generally >200/cumm. HIV associated cardiomyopathy has poor prognosis. Other findings on echocardiography may be diastolic dysfunction, pericardial effusion, right ventricular hypertrophy, pulmonary arterial hypertension and non-bacterial thrombotic endocarditis.

GASTROINTESTINAL MANIFESTATIONS

Manifestations of gastrointestinal tract can be due to HIV itself or drugs used in the treatment. Aphthous ulcers are generally found in posterior oropharynx and oesophagus. Ulcers produce dysphagia and severe odynophagia due to ulcerative oesophagitis. These lesions can be present in cases of severe immunodeficiency or during seroconversion. Several

studies have demonstrated HIV infected inflammatory cells in the base of these lesions suggesting aetiological role of HIV. Endoscopically one or multiple ulcers of variable depth with normal intervening mucosa may be present, as seen in CMV infection. Short-term steroids or thalidomides are effective. Relapse rate of these ulcers is high. Other gastric problems are generally rare.

AIDS ENTEROPATHY

Direct involvement of intestine by HIV can cause AIDS enteropathy or HIV enteropathy. Features include villous blunting, low mitotic figures and decrease in villous-crypt ratio. Patients usually present with chronic diarrhoea and weight loss. Stool studies, sigmoidoscopy and/or upper gastrointestinal endoscopy should be done to rule out other aetiologies. Tests of malabsorption are deranged. Treatment includes non-specific management like dietary fibre supplementation, antimotility agents, octreotide and oral rehydration solution.

HEPATOBILIARY MANIFESTATIONS

Direct involvement of liver parenchyma by HIV is not documented, and most common cause of hepatic involvement is co-infection with hepatitis B, C and administration of antiretroviral therapy. In India hepatitis B co-infection is present in 2% to 9 % cases and hepatitis C in 2% to 3%.

Intravenous drug users may have HCV co-infection in up to 50% to 90%. Drugs like nevirapine, protease inhibitors (atazanavir) can cause severe acute hepatitis or hepatic failure and their use should be properly monitored.

AIDS cholangiopathy is a syndrome resembling sclerosing cholangitis with papillary stenosis. Diagnosis is made by ERCP and papillotomy can relieve obstruction.

NEUROLOGICAL MANIFESTATIONS

Neurological diseases due to direct HIV infection occur throughout the course of infection and may be due to basic pathology like inflammation, demyelination or degeneration.

AIDS-Dementia Complex (HIV Encephalopathy)

It is an AIDS defining illness and usually occurs at CD4+ counts >200/cumm. If untreated, 15% to 20% of HIV patients will develop this entity. AIDS-dementia complex (ADC) or HIV encephalopathy (HIVE) is the term used to describe the advanced neurological involvement. HIV infects macrophages and glial cells in central nervous system. Release of various cytokines/neurotoxins such as interleukin (IL)-1β, tumour necrosis factor-α, IL-6 and TGF-β may be responsible for involvement of neuronal cells. HIV encephalopathy is a slowly progressive subcortical dementia.

Typical complaints are forgetfulness, poor concentration, slowing of reasoning, lack of energy drive, mild depression and emotional blunting. Patients look apathetic and slow and become socially withdrawn. Sexual dysfunction is common. Signs of HIV encephalopathy include impaired gait, slowing of rapidly alternating movements, tremor, brisk deep tendon reflexes, positive Babinski sign, slowed gaze saccades, sphincter impairment including incontinence and frontal release signs.

Neuropsychological findings such as slowing of psychomotor speed, impaired short-term memory and mental flexibility, problem with recalling events in correct order, disorientation to time, place and person and finally mutism can occur. MRI is preferred imaging modality. It reveals patchy or diffuse, hyperintense and relatively symmetrical lesions of white matter suggestive of leucoencephalopathy. Cerebrospinal fluid examination should be done to exclude alternative diagnosis. A systematic mental status examination is an important part of the examination. Quantitative neuropsychological tests can be done to see progressive decline in neurological functions. Metabolic disorders, depression and anxiety should be ruled out. Antiretroviral therapy should be optimised. Highly CNS penetrant drugs should best be used from the list of lamivudine, zidovudine, nevirapine and indinavir. Outlook for prolonged independent life is guarded.

HIV Myelopathy

Myelopathy is present in 20% patients with AIDS. Vacuolar myelopathy is pathologically similar to subacute combined degeneration of cord. The histological hallmark are vacuoles and lipid laden macrophages most prominent is cervical and thoracic spinal cord. It is characterised by insidious onset of leg weakness and gait abnormalities. Vague leg discomfort and paraesthesias are main sensory symptoms. Bladder and bowel dysfunction is also common. Posterior columns of cord can also be separately involved producing pure sensory myelopathy and pure sensory ataxia. MRI of spinal cord is usually normal. Treatment of myelopathy with ART is not much rewarding.

Peripheral Neuropathy

It can present like acute inflammatory demyelinating polyneuropathy resembling GB syndrome. Chronic inflammatory demyelinating polyneuropathy (CIDP) with relapsing and remitting course has also been documented. Distal sensory neuropathy is most common type of neuropathy which can be due to HIV itself or nucleoside analogue drugs. Mononeuritis multiplex can also be present. Pregabalin, carbamazepine,

gabapentin, tricyclic antidepressant and analgesics can provide symptomatic improvement.

HAEMATOLOGICAL MANIFESTATIONS

Anaemia is the most common haematological finding. Normocyctic normochronic anaemia is found in HIV-associated bone marrow suppression. Reticulocyte count is inappropriately low. Drugs like zidovudine is the other main culprit. It can block erythroid maturation earlier than other components of bone marrow. Mean corpuscular volume of RBC is increased. HIV-induced anaemia may respond well to ART therapy. Erythropoietin is also effective if its levels are less than that expected for severity of anaemia. Zidovudine should be replaced. Neutropenia is mostly mild but sometimes it can be severe. The cause of neutropenia can be a direct effect or therapy induced. Presence of neutropenia generally indicates advanced disease. G-CSF or GM-CSF can be of use in increasing counts of neutrophils regardless of the cause. Myelosuppressive drugs should be removed. Thrombocytopenia can be due to decreased platelet survival probably by immunological mechanism and decreased platelet production due to infection of megakaryocytes with HIV.

Treatment should be initiated in patients having platelet count <20000/cumm. IVIG and Anti Rh(D) are equally effective but sustained

responses are few. Prednisolone 0.5-1.0 mg/kg is used cautiously. Splenectomy may be needed in relapsed/refractory cases.

Persistent generalised lymphadenopathy is an early clinical presentation of body response to HIV infection. The condition is defined as lymph node enlargement of 2 or more extrainguinal sites of size >1 cm for at least more than 3 months without obvious cause. Histologically follicular hyperplasia of lymph nodes is present.

RENAL MANIFESTATIONS

HIV-associated nephropathy (HIV-AN) is a true direct complication of HIV infection occurring in 2% to 10% of HIV infected individuals. Clinical presentations of HIV-AN consist of heavy proteinuria (90% have nephritic range), rapid deterioration of renal function, normal size of kidneys, no or minimal increase in blood pressure. End stage renal disease commonly occurs in 6 to 12 months. Kidney biopsy is diagnostic. Histology is similar to that of idiopathic focal segmental glomerulosclerosis (80%) and mesangial proliferation in 10% to 15% cases. HIV-AN also exhibits sclerosis of the whole glomerular tuft which is distinctly known as collapsing glomerulopathy. Majority of patients have CD4+ T-cell counts <200/cumm. ACE inhibitors and prednisolone with tapering dose have been effective in preventing progression of the disease. IgA nephropathy can also occur in HIV patients. Acute tubular necrosis

can result from nephrotoxic drugs, hypovolaemia, shock and sepsis. Drugs like pentamidine, amphotericin, adefovir, tenofovir, NSAIDs and radiocontrast agents can cause acute tubular necrosis. Patient should be closely monitored and dose adjustments or stoppage of drug should be considered once renal dysfunction develops.

HIV-Associated Wasting

It is an AIDS defining illness. Center for Disease Control and Prevention (CDC) definition of HIV-associated wasting is a weight loss of >10% associated with intermittent or constant fever and chronic diarrhoea or fatigue lasting >30 days in the absence of a defined cause other than HIV infection. Dietary assessment and weight monitoring should be done. Key to prevention and management of HIV wasting is aggressive management of infection.

PULMONARY MANIFESTATIONS

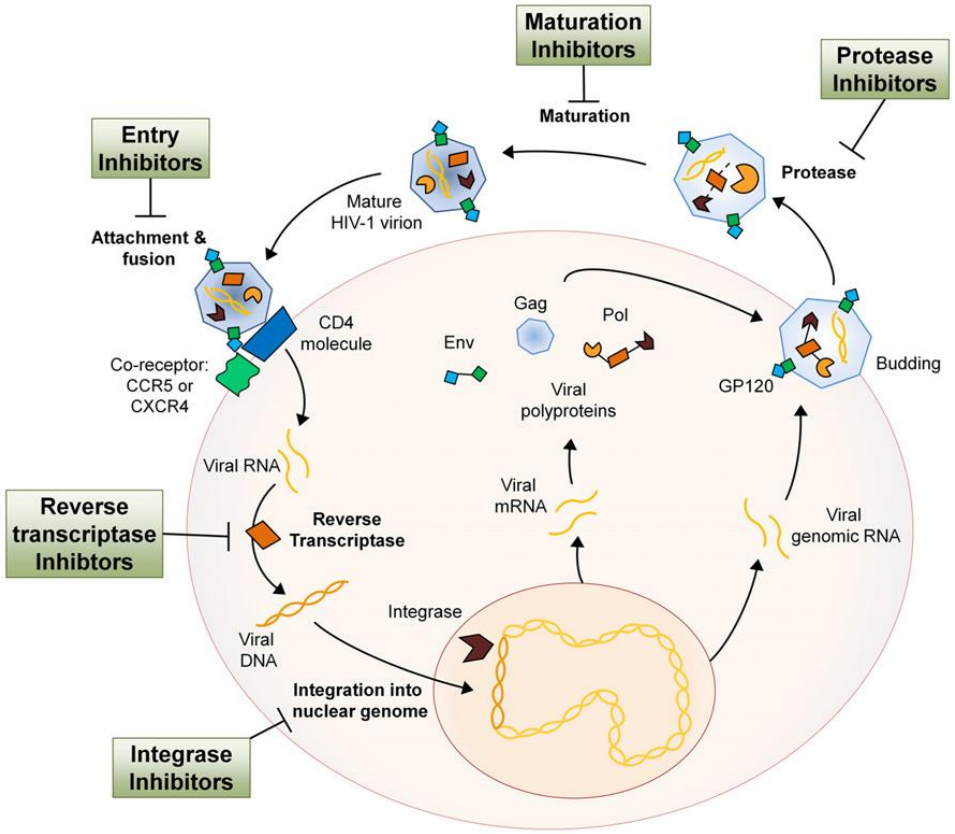
Most of the pulmonary manifestations are due to opportunistic infections and should be ruled out before attributing it to HIV disease. Lymphocytic interstitial pneumonia, non-specific interstitial pneumonia and increased incidence of pulmonary hypertension is seen as the non-opportunistic infection manifestations of HIV disease.

TREATMENT

ANTIRETROVIRAL THERAPY

The advent of antiretroviral drugs in the early 1990s began a revolution in the management of HIV infection. Results from various trials [13] involving different drug combinations showing their efficacy opened the opportunities to reduce the morbidity and mortality due to HIV/AIDS. The combination of atleast three antiretroviral drugs from different groups is the current standard of care and is commonly referred to as highly active antiretroviral therapy (HAART). There is enough epidemiological and clinical evidence that effective combinations of antiretroviral drugs inhibit the replication of HIV and reduce viraemia to undetectable levels. Treatment slows down the disease progression, improves the quality of life and increases the longevity. Success achieved by antiretroviral therapy (ART) has now transformed the common perception about HIV infection from being a ‘virtual death sentence’ to a ‘chronic manageable illness’.

NRTI	NNRTI	Protease inhibitors	Fusion inhibitors
Zidovudine (AZT)	Efavirenz (EFV)	Ritanovir (RTV)	Enfuvirtide
Lamivudine (3TC)	Nevirapine (NVP)	Saquinavir (SQV)	
Emtricitabine (FTC)	Delavirdine (DLV	Indinavir (IDV)	
Stavudine (d4T)		Nelfinavir (NFV)	
Didanosine (ddI)		Fosamprenavir (APV)	
Tenofovir (TDF)		Lopinavir (LPV)	
Abacavir (ABV)		Atazanavir (ATV)	
Zalcitabine (ddC)		Darunavir (DRV)	



GOALS OF ANTIRETROVIRAL THERAPY [14]

The primary goals of ART are maximal and durable reduction in plasma viral levels and restoration of immunological functions. The reduction in viral load also leads to reduced transmissibility. However, as yet there is no therapy to eradicate HIV from the body. Antiretroviral (ARV) drugs can also be used to reduce the risk of vertical transmission. The ARVs can be used after exposure to HIV too, as in cases of accidental needle stick injury, and in cases of sexual assault and rape. It is called post-exposure prophylaxis (PEP).

The management of HIV is becoming increasingly complex in view of long-term toxicity, drug-to-drug interaction and drug resistance. In addition, monitoring facilities such as CD4 counts, viral load estimation and drug resistance assay have become necessary for follow-up.

PRINCIPLES OF ANTIRETROVIRAL THERAPY

A continuous high level of replication of HIV takes place in the body right from the early stages of infection. At least one billion viral particles are produced and destroyed each day. The antiretroviral drugs act on various stages of replication of HIV in the body and interrupt the process of viral replication. Most commonly used drugs target the virus mainly by

inhibiting the enzymes reverse transcriptase inhibitors and protease inhibitors. Based on the scientific evidence, therapy guidelines have been developed by various international agencies such as WHO. They define the optimum time, parameters and drugs to initiate and sequence treatment. Since, the drug therapy is lifelong, the selection of patients for therapy is based on clinical, immunological and viral parameters. Patients preparedness for such a prolonged therapy and monitoring ensures their adherence. Oppurtunistic infections (OIs), if any, should be treated first. Patients should undergo therapy counselling. Along with detailed clinical evaluation, co-morbid conditions such as hepatitis B virus (HBV), hepatitis C virus (HCV) need to be evaluated for proper selection of ARVs considering the efficacy and drug interactions.

PREVIOUS STUDIES

STUDY 1 [15]

Thinyane et al conducted a prospective observational study, **Clinical Profiles of HIV-Infected, HAART-Naive Patients Admitted to a Tertiary Level Hospital in Maseru, Lesotho**, at Queen Elizabeth II (QE II) Referral Hospital in Maseru, Lesotho in South Africa a high prevalent country for HIV. QEII Hospital is a public sector tertiary level hospital which also functions as the national referral hospital. The study population included consecutive 105 adult patients (> 15 years) wards between July and October 2010. Patients were included if they tested positive for HIV(either known to be people living with HIV prior to admission or tested positive following admission), not receiving highly active anti-retroviral therapy (HAART) and admitted for the treatment of HIV-related disorders.

The most common symptom was cough which was followed by weight loss or wasting and generalised weakness. The commonest opportunistic infection was tuberculosis which was followed by oral candidiasis and pneumonia. The most common non-infectious HIV-related disease was anaemia. 5 patients were diagnosed with symptomatic HIV associated

nephropathy and 1 patient with Kaposi Sarcoma .59% were in Stage 3 and 41.0% were in Stage 4 of HIV infection. More than two thirds of the study participants had anaemia.

STUDY 2 [16]

Nashaba et al did a study on **Clinical Profile of HIV/AIDS-infected Patients admitted to a New Specialist Unit in Dhaka, Bangladesh - A Low-prevalence Country for HIV**. This was a retrospective study on HIV positive patients admitted in a hospital in Dhaka. The aim of the study was to find the common opportunistic infections prevalent in HIV positive patients in that population and the status of CD4 count in them. Most of the population studied were adults (>94%). Tuberculosis was the most common opportunistic infection which was found in the study population. Others common opportunistic infections were oral or oesophageal candidiasis , pulmonary infections and herpes zoster. Other common clinical manifestations of the disease recorded were weight loss, diarrhoea, lymphadenopathy and fever. With respect to CD4 count data, the largest number of patients was in the group with CD4 counts from 51to 200 cells/μL which constituted 31%. The next largest group had CD4 counts of above 350 cells/μL which constituted 26%. Although those with a CD4 count of <50 cells/μL represented 24% of the cohort, 62% of deaths were

in this group of patients, indicating high morbidity and mortality associated with low CD4 counts, as reported in various other studies.

STUDY 3

Chakaravarthy et al conducted a study on on **Clinico-epiemiological Profile of HIV Patients in Eastern India**

In this study, 438 HIV positive patients attending the outpatient clinic of Sir Sundar Lal Hospital, Institute of Medical science, Banarus Hindu University were enrolled. Of these 354 were males (mean CD4 count 179 ± 9.3 cells/µl) and 84 were females (mean CD4 count 323 ± 28.26 cells/µl). The average age of the study subjects during the time of diagnosis was 32.6 years. The commonest mode of transmission was heterosexual contact in 80.4% patients followed by blood transfusion in 2.5%. Among the male patients, 71.5% were found to be migrant workers. Fever (70.6%), weight loss (53.3%), chronic diarrhea (43.9%) and cough (40.3%) were the common presenting symptoms. Out of the 438 patients, 66.4% had opportunistic infections at the time of reporting to the hospital. The most common opportunistic infection was tuberculosis (38.8%) which was followed by oropharyngeal candidiasis (20.3%) and diarrhea (12.7%). CD4 count was inversely proportional to the number of symptoms and opportunistic infections.

STUDY 4 [17]

Kaiser et al conducted a study on **Clinical Profile of HIV/Aids Patients in Srinagar, Kashmir, India.**

The aim of the study was to assess the number of seropositive HIV patients enrolled in Government medical college and other associated hospitals in Srinagar, Kashmir, India, common signs and symptoms , age and sex distribution, modes of transmission and different types of opportunistic infections. The mean age of these patients were found to be 34.45±8.40 with a higher male is to female ratio at 7:1.The summit incidence was found in the age group of 30-39yrs of age. Major group of HIV positive patients belonged to patients working as security personnel followed by migrant labourers and housewives. Sexual transmission was the main mode of transmission (90.7 %)followed by homosexual transmission (4.7 %). 78.9 % of patients had fever of greater than 1 month duration, 35.1 % had weight loss and 33.5% had diarrhoea. Tuberculosis and oral/esophageal/genital candidiasis were the most common opportunistic infection followed herpes zoster and varicella zoster.

STUDY 5 [18]

Jayant et al conducted a study on **Clinico-epidemiological profile of HIV patients attending ART centre in rural Western Maharashtra, India**, which was a cross-sectional study, conducted at ART centre of a rural tertiary care hospital, situated in Maharashtra, India, from the March of 2011to September 2011. The study revealed that the most common presenting complaints were weight loss, fever, cough, and chronic diarrhoea. The majority of the patients in the study belonged to the sexually active age group of 20 to 40 years of age. Heterosexual contact was the commonest mode of acquiring the infection. Tuberculosis (62%) was the most common opportunistic infection which was followed by pneumosystis carinii pneumonia, herpes zoster, malignancy, candidiasis, neurological disorders and ophthalmic manifestations. It was found that as the CD4 count decreased, incidence and the number of opportunistic infections in patients increased. As per the WHO staging 42.5% patients were in stage 3

MATERIALS AND METHODS

MATERIALS:

100 randomly selected newly diagnosed HIV infected patients attending the ART centre, Tirunelveli Medical College, Tirunelveli.

DURATION OF THE STUDY: 1 YEAR

TYPE OF STUDY: DESCRIPTIVE STUDY

SAMPLE SIZE: 100

INCLUSION CRITERIA:

- >15 years of age
- HIV seropositive
- Newly registered in ART centre at TVMCH between June 2014 to may 2015
- Not on HAART

EXCLUSION CRITERIA:

- <15 years of age
- Already on HAART

METHODOLOGY:

Informed consent was obtained for taking part in this study. Patient information, medical history including diagnosis of HIV-infection, opportunistic infections and other HIV-related disorders was obtained from the patient medical records using predesigned data collection forms.

Clinical staging of patients was done based on the World Health Organisation (WHO) criteria for the Clinical Staging of Established HIV Infection.

Investigations included full blood count, liver function tests, renal function tests and CD4 count.

STATISTICAL ANALYSIS

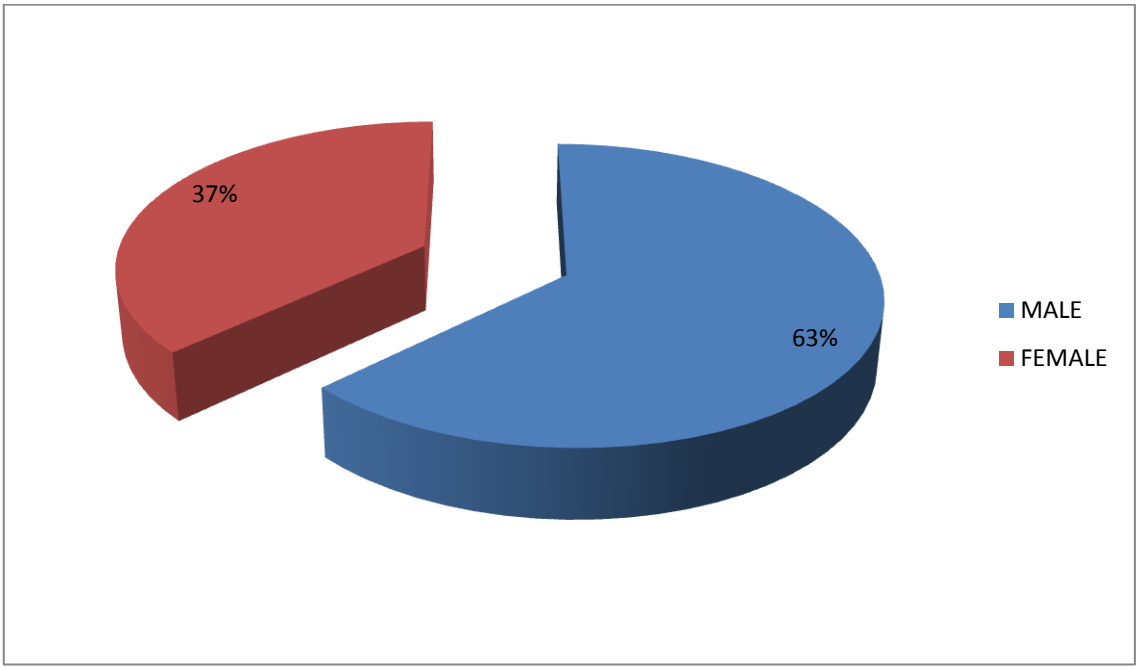
Statistical analysis was done using simple percentage analysis.

OBSERVATIONS

AND

RESULTS

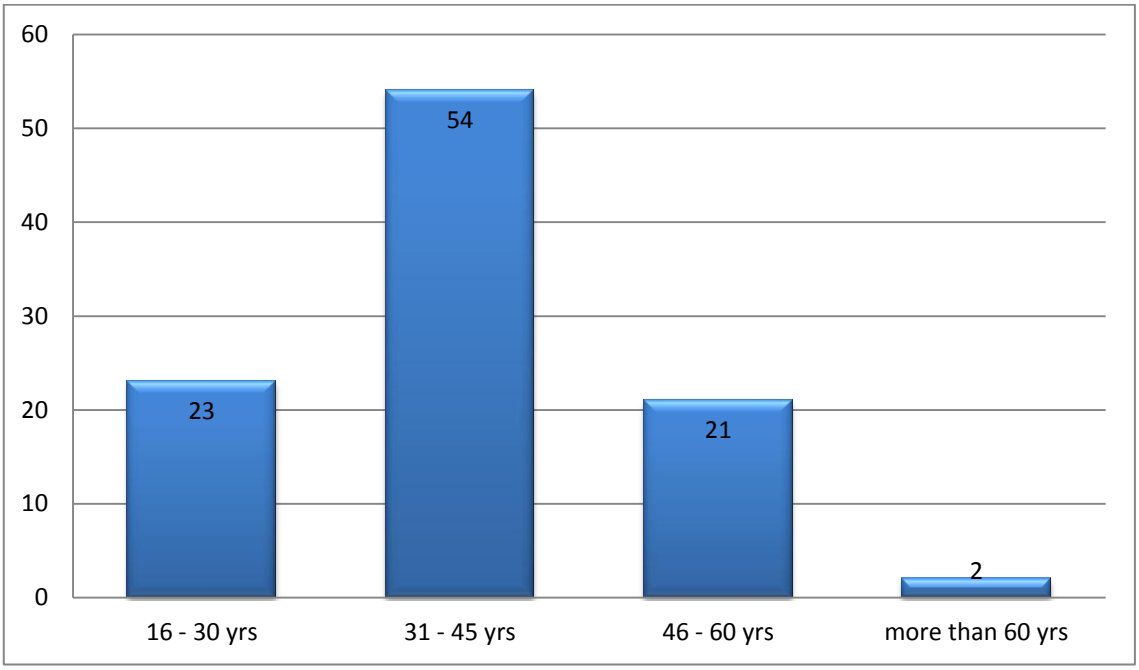
SEX DISTRIBUTION



GENDER	NUMBER	PERCENTAGE
MALE	63	63
FEMALE	37	37

In this study the number of males (63%) included in the study was more than the females (37%).

AGE DISTRIBUTION

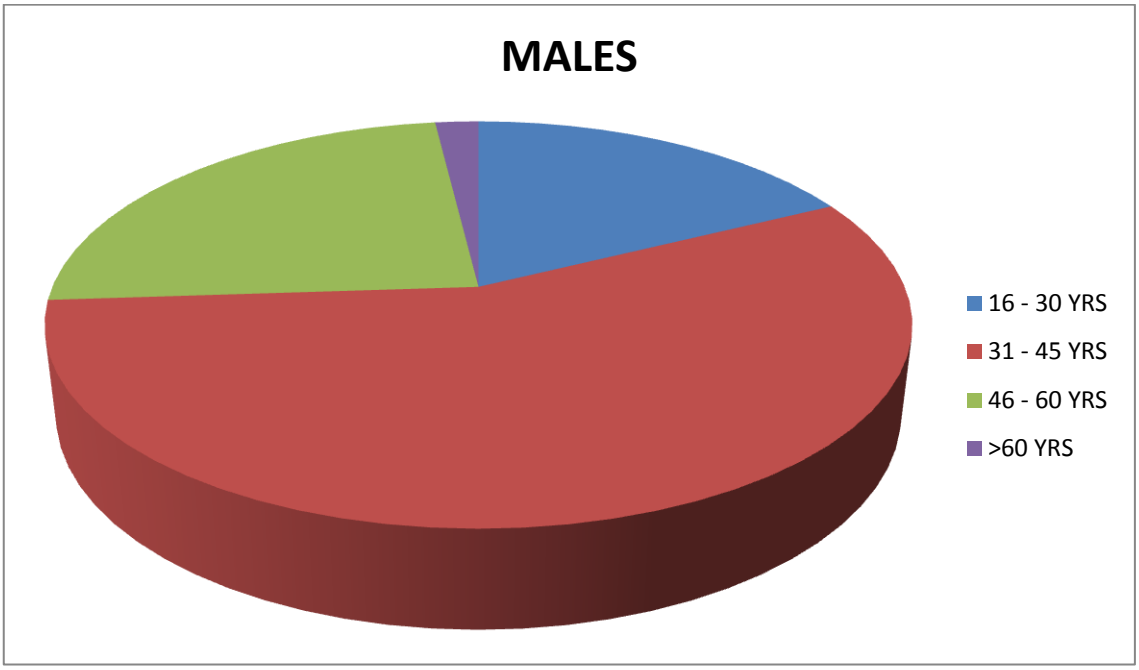


AGE RANGE	NUMBER	PERCENTAGE
16 – 30 YRS	23	23
31 – 45 YRS	54	54
46 – 60 YRS	21	21
MORE THAN 60 YRS	2	2

More than half of the population in the study were in the age group of

31 to 45 years of age.

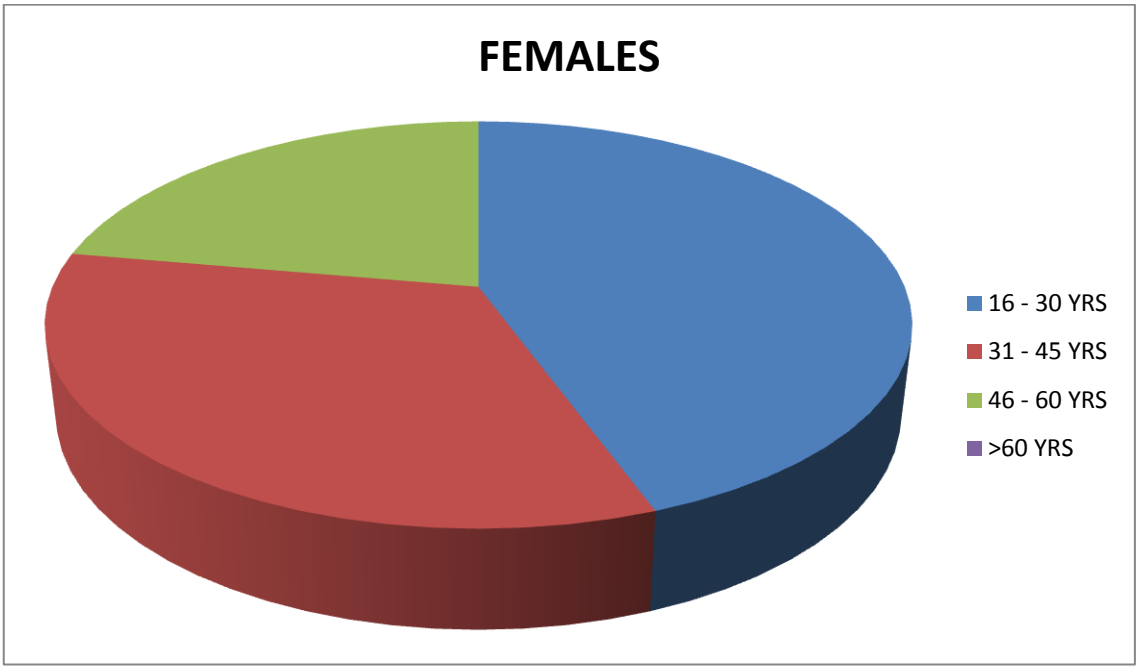
SEX AND AGE RELATIONSHIP (MALES – PERCENTAGE)



AGE RANGE	NUMBER	PERCENTAGE
16 – 30 YRS	11	17.46
31 – 45 YRS	35	55.55
46 – 60 YRS	15	23.80
MORE THAN 60 YRS	2	3.17

Out of the number of males studied, 55.55% were in the age group of 31 to 45 years of age.

SEX AND AGE RELATIONSHIP (FEMALES - PERCENTAGE)

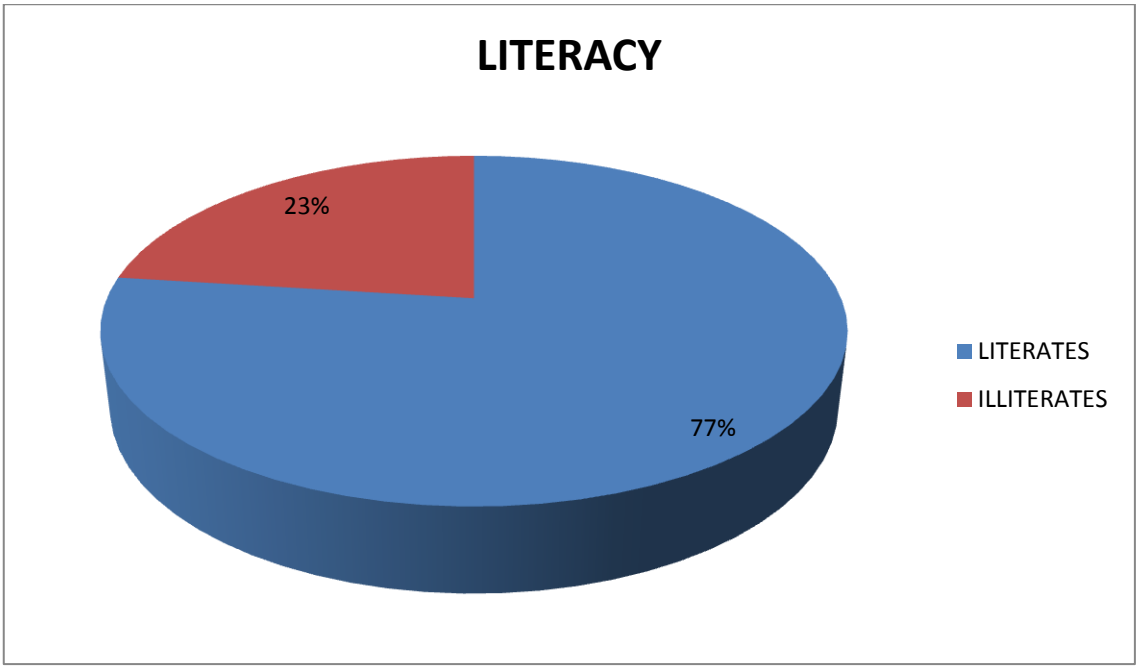


AGE RANGE	NUMBER	PERCENTAGE
16 – 30 YRS	12	32.43
31 – 45 YRS	19	51.35
46 – 60 YRS	6	16.21
MORE THAN 60 YRS	0	0

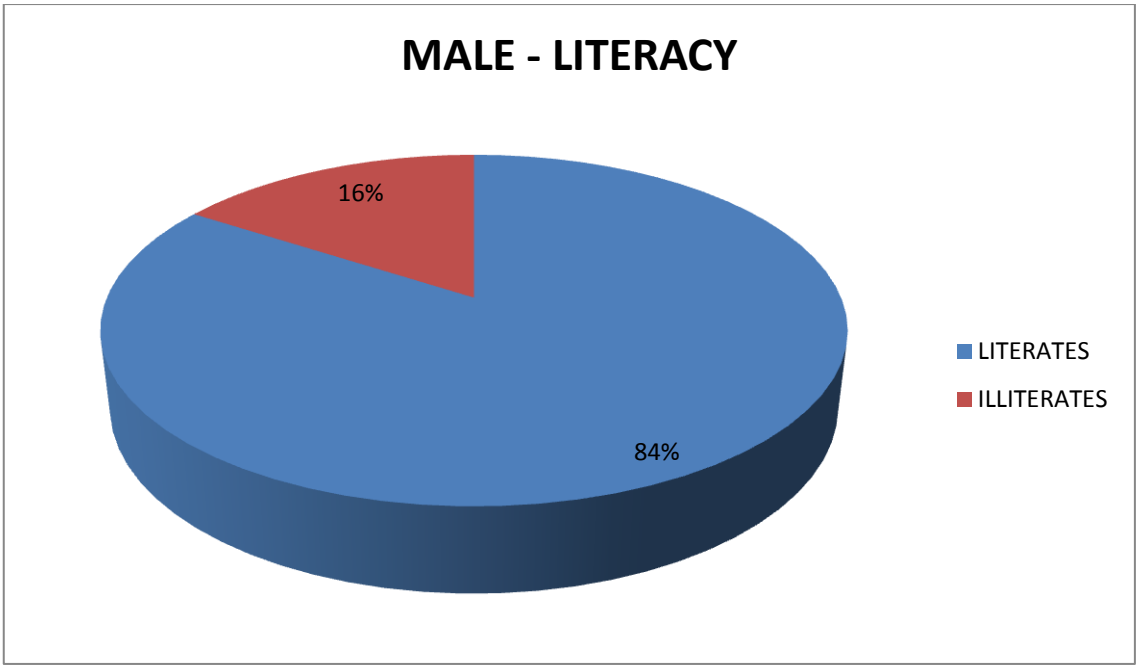
More than half of the females were in the age range of 31 to 45 yrs of age.

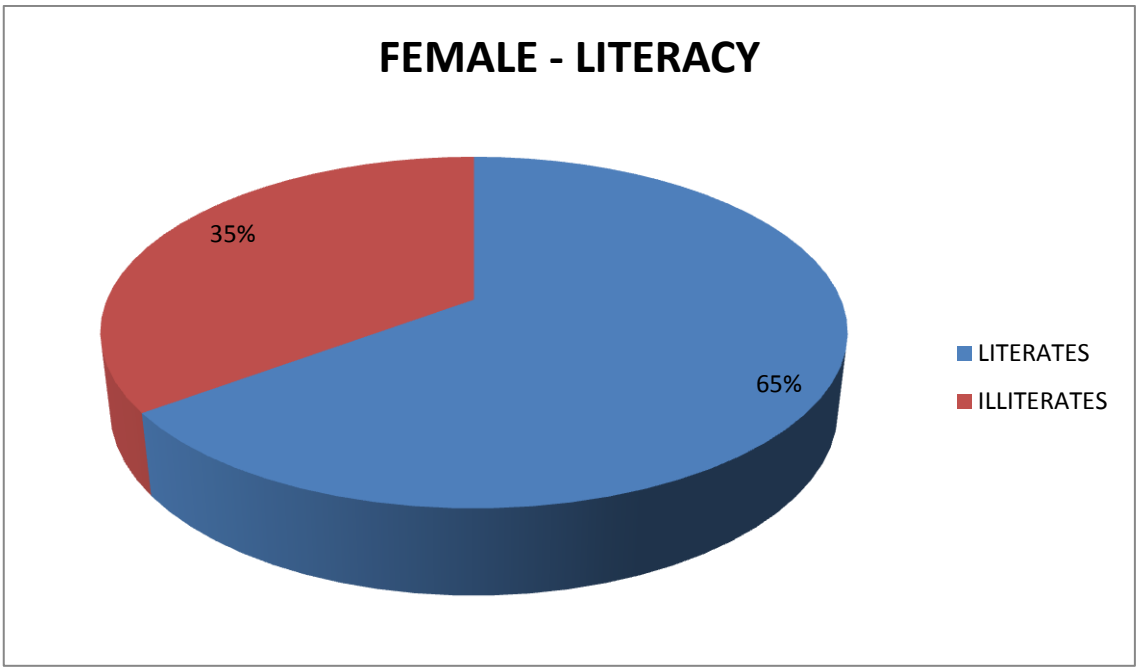
LITERACY – FREQUENCY DISTRIBUTION

LITERACY	MALE	FEMALE	TOTAL
LITERATES	53	24	77
ILLITERATES	10	13	23



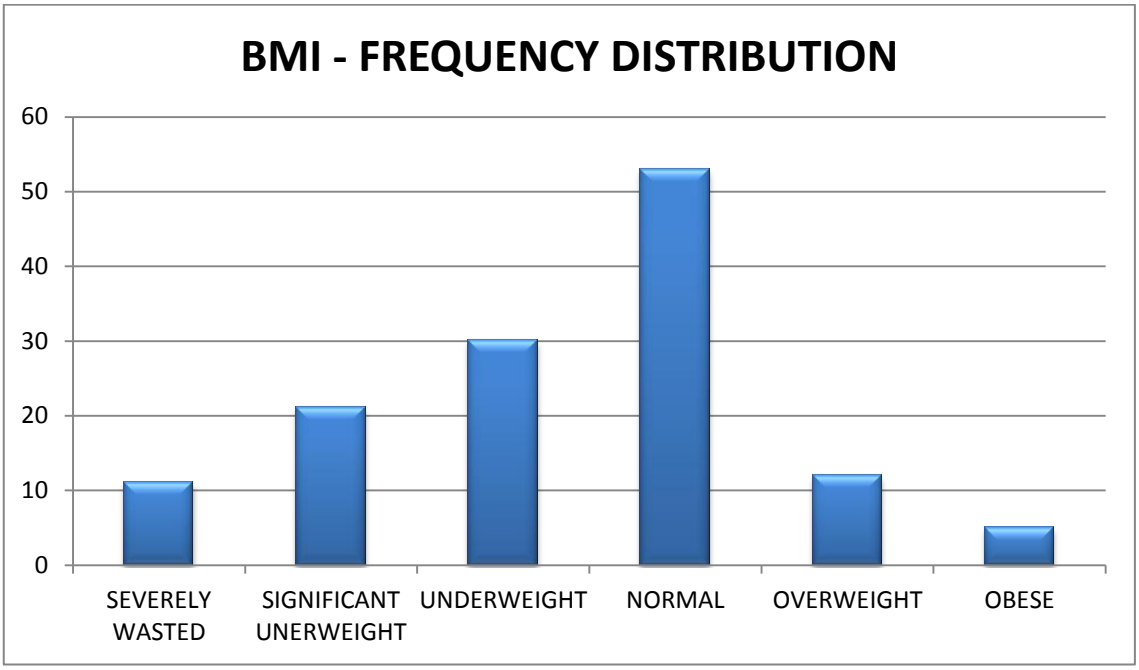
About 77% of the patients were literates and the rest were illiterates.



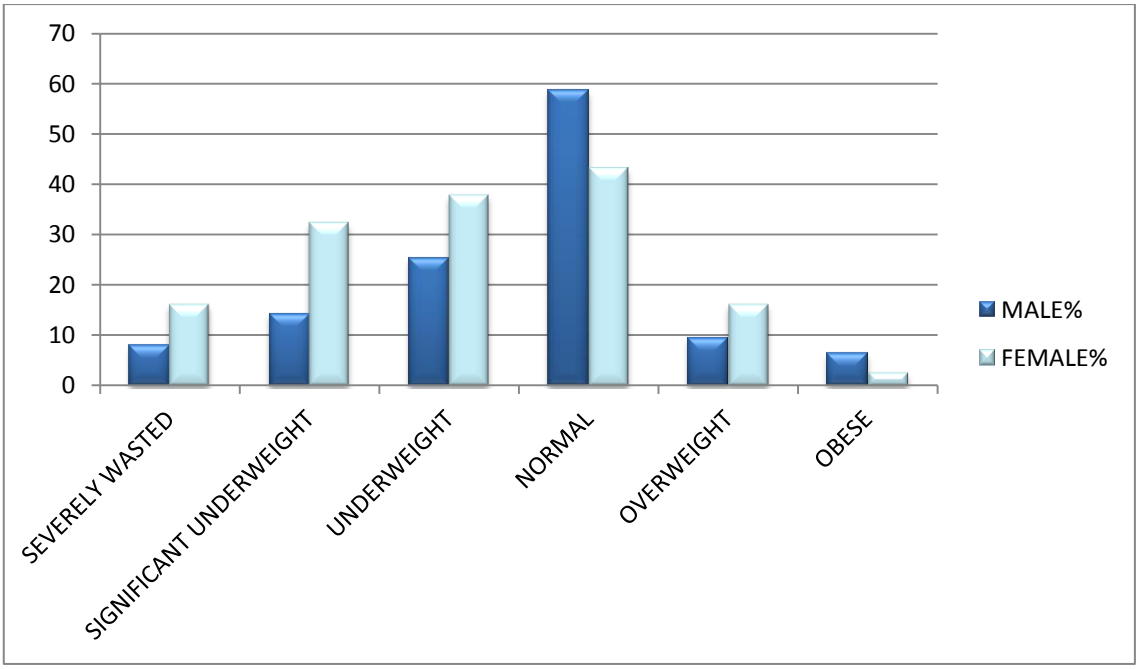


The percentage of illiteracy was more in the females when compared to the males within the study group.

BODY MASS INDEX FREQUENCY DISTRIBUTION



BMI – SEX FREQUENCY DISTRIBUTION



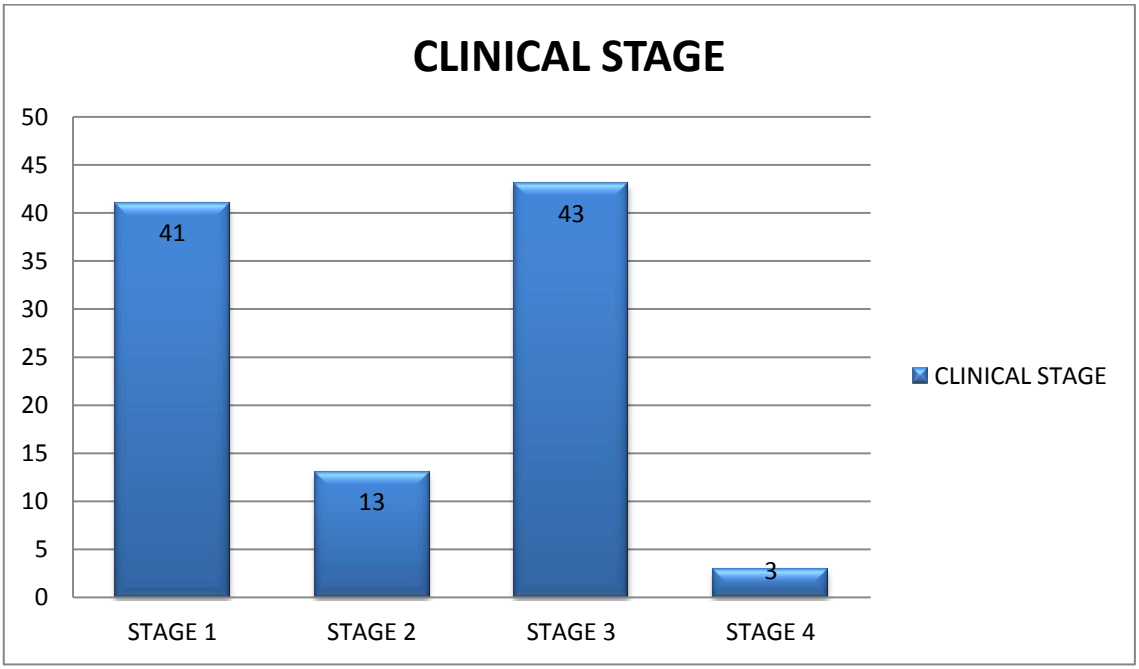
RANGE	MALE		FEMALE		TOTAL	
	NUMBERS	%	NUMBERS	%	NUMBERS	%
<16(Severely wasted)	5	7.9%	6	16.2%	11	11%
<17(Significant underweight)	9	14.3%	12	32.4%	21	21%
<18.5(Underweight)	16	25.3%	14	37.8%	30	30%
18.5 to 24.9 (Normal)	37	58.7%	16	43.2%	53	53%
25 to 29.9 (Overweight)	6	9.52%	6	16.2%	12	12%
>30 (Obese)	4	6.34%	1	2.7%	5	5%

After applying the WHO BMI classification 30% of the study group were found to be underweight, 21% were significantly underweight and 11% were severely wasted.

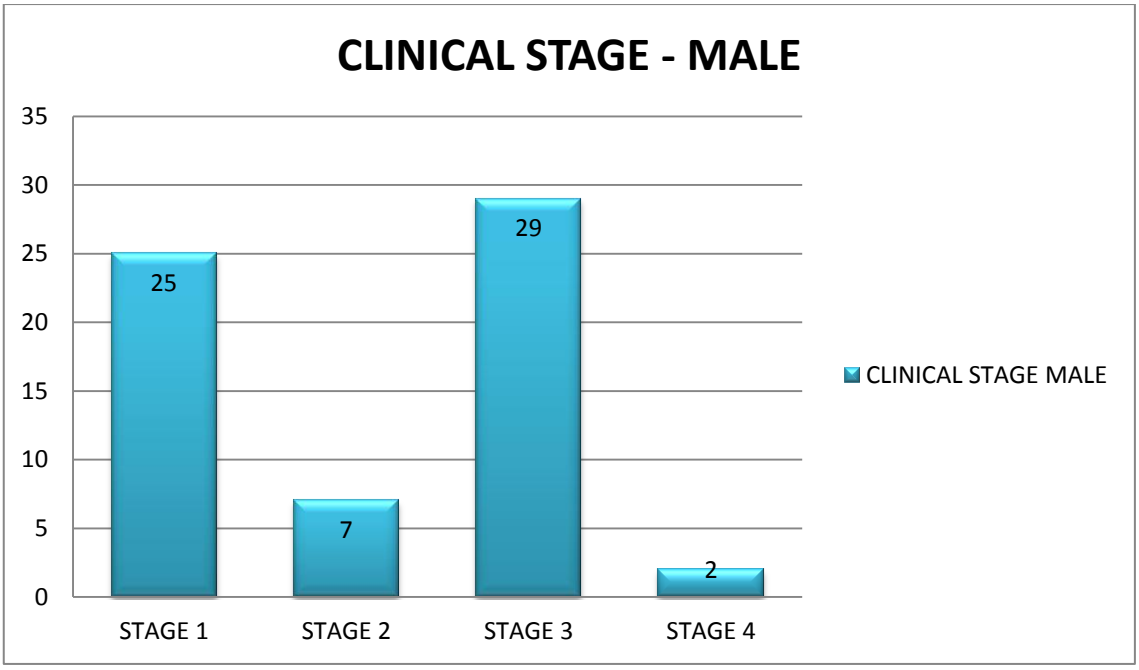
37.8% of females were found to be underweight compared to 25.3% of males.

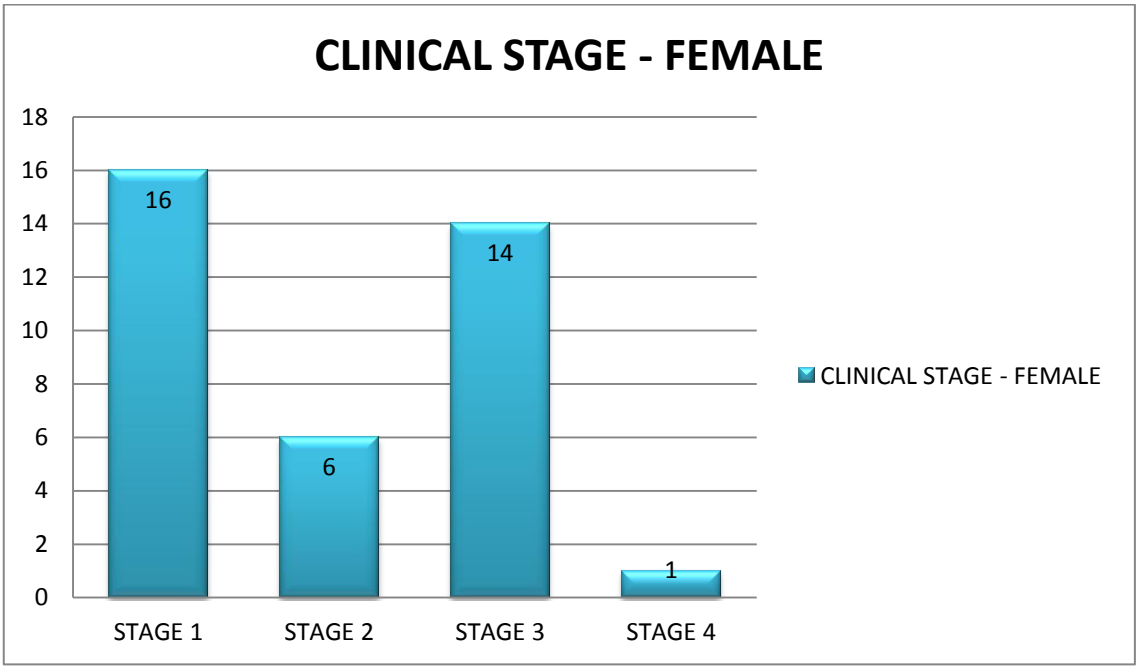
CLINICAL STAGE FREQUENCY DISTRIBUTION

CLINICAL STAGE	MALE	FEMALE	TOTAL
STAGE 1	25	16	41
STAGE 2	7	6	13
STAGE 3	29	14	43
STAGE 4	2	1	3



41% of the study group population were asymptomatic (Stage 1). 43% of them were in the clinical stage 3. Only 3% were in the clinical stage 4.



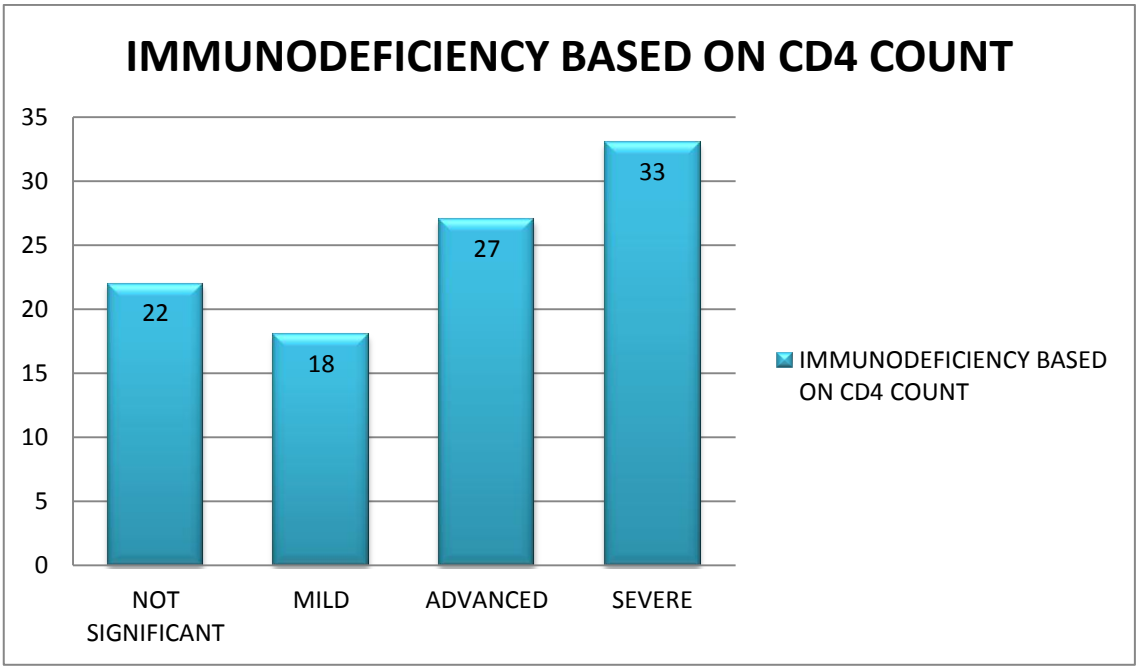


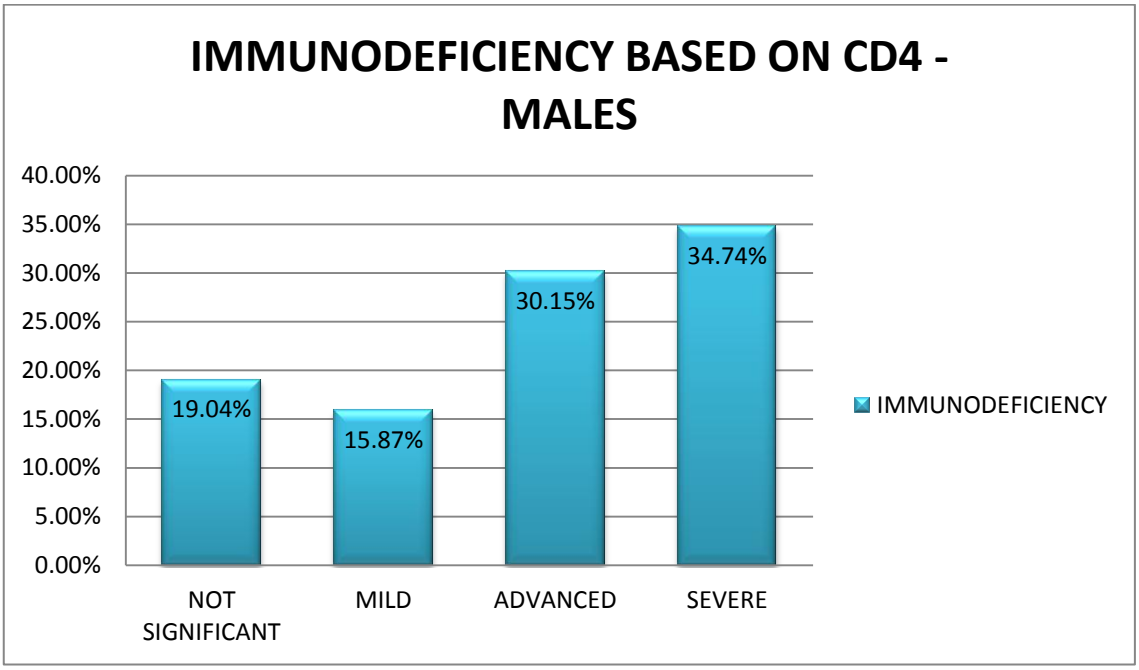
The distribution of clinical stage among males and females in the study population showed relatively similar trend.

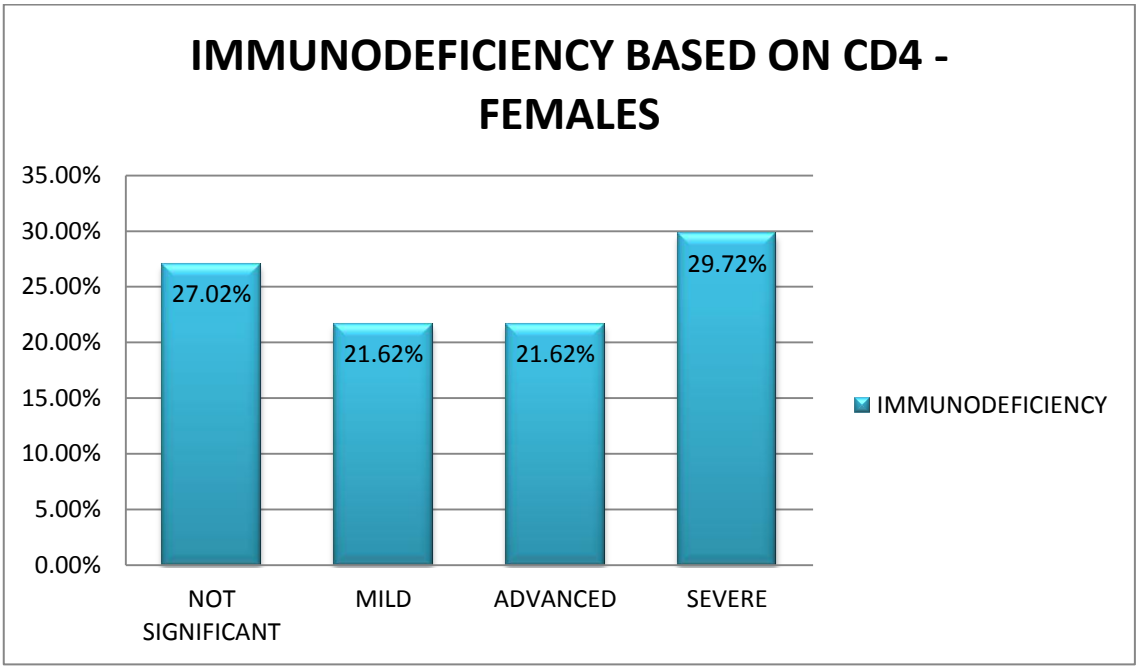
HIV ASSOCIATED IMMUNODEFICIECY BASED ON CD4 COUNT

(Based on WHO immunological classification for established HIV infection)

IMMUNODEFICIENCY	CD4 VALUE	MALE	FEMALE	TOTAL
NOT SIGNIFICANT	>500	12	10	22
MILD	350 - 499	10	8	18
ADVANCED	200 - 349	19	8	27
SEVERE	<200	22	11	33

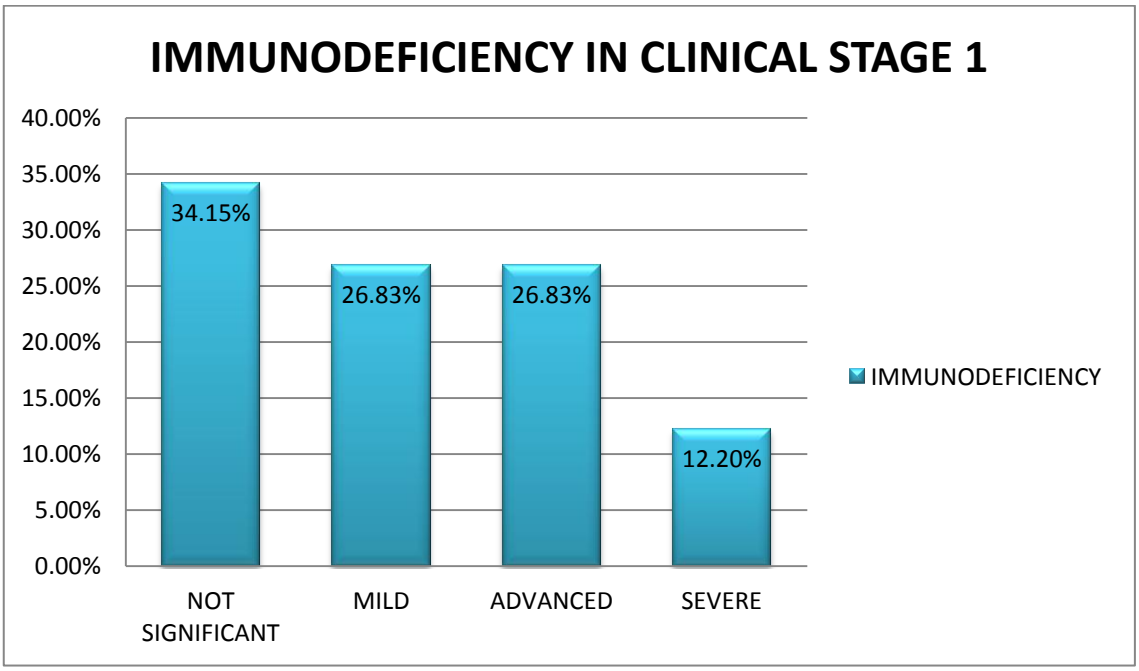




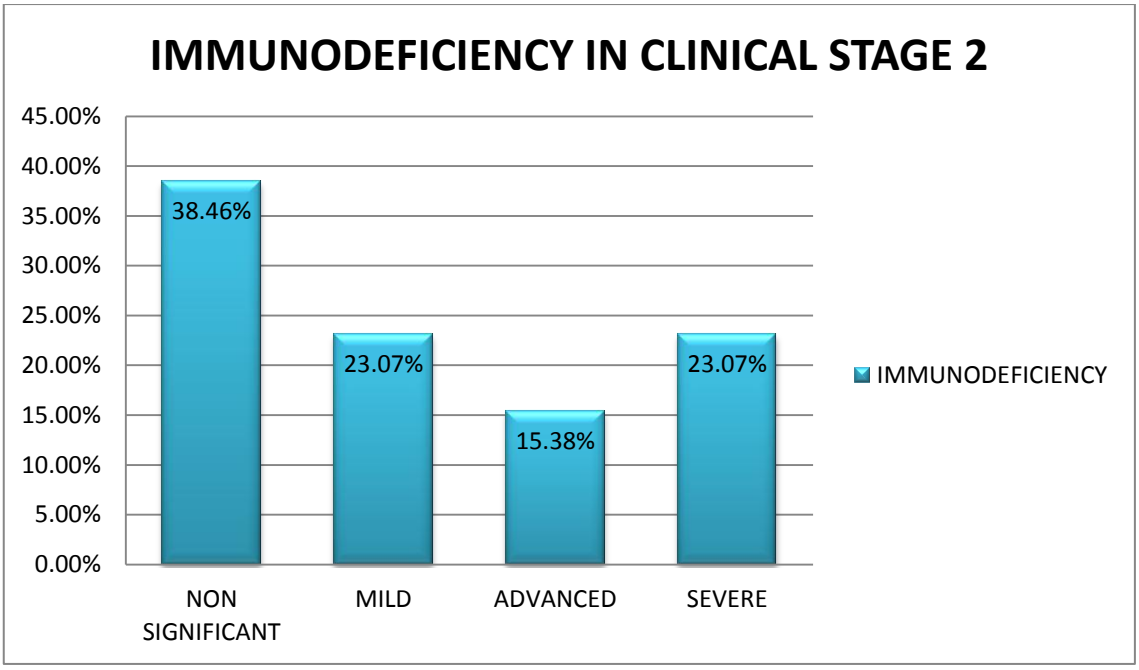


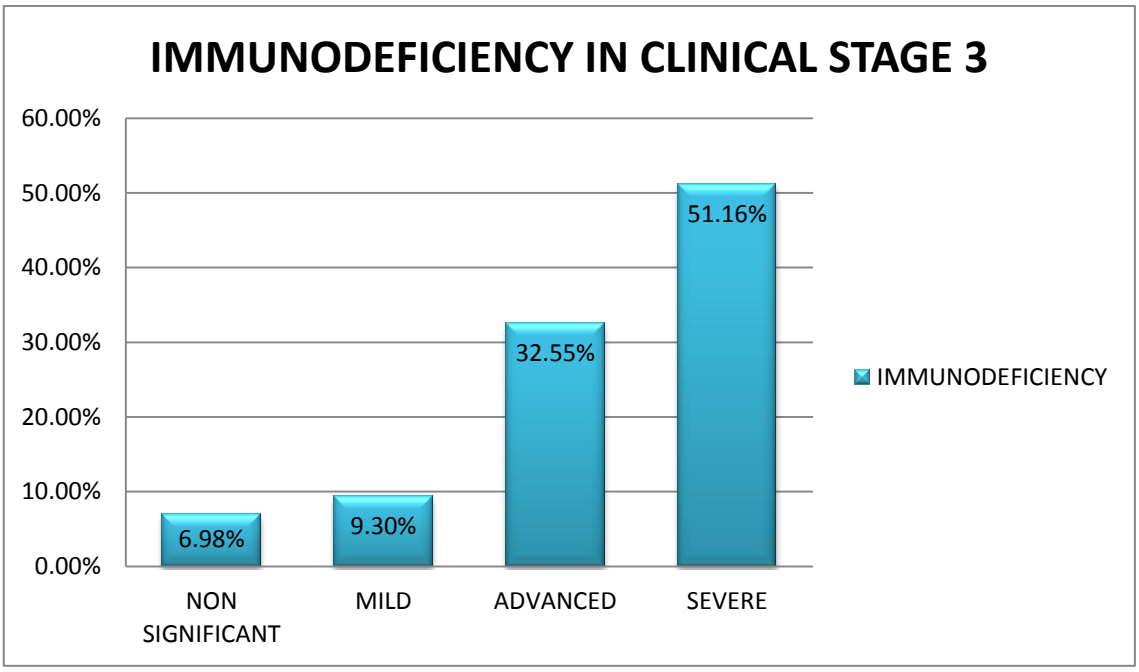
Although only three percentage of the study population fall into clinical stage 4, based on CD4 counts 33 percentage of study population are having severe immunodeficiency.

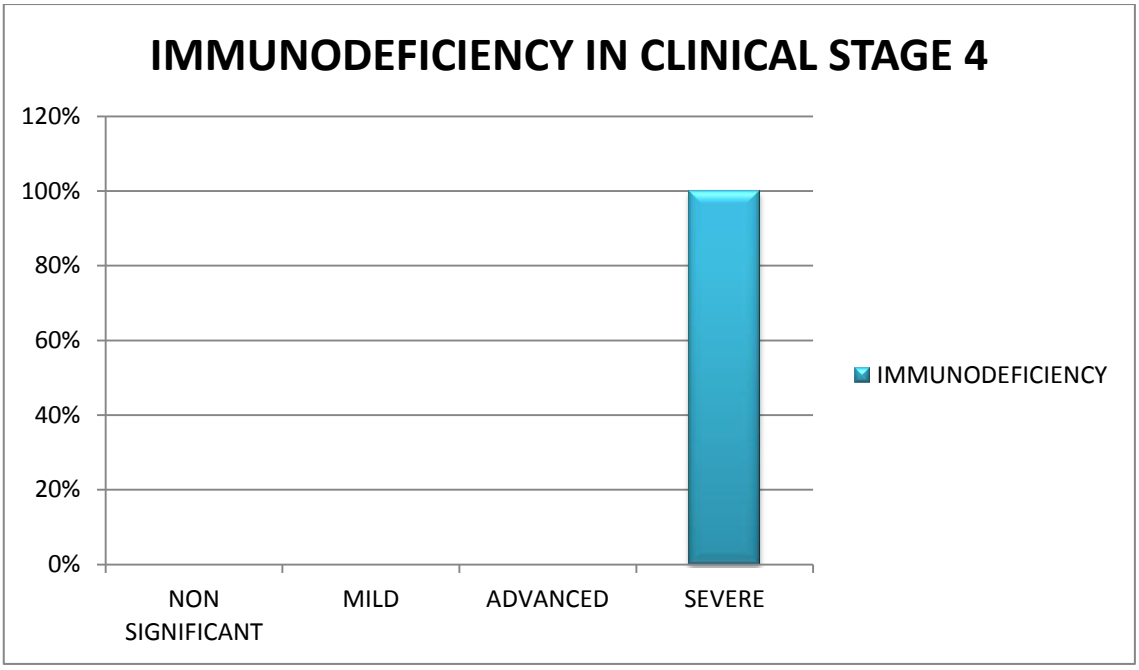
DISTRIBUTION OF IMMUNODEFICIENCY AMONG VARIOUS CLINICAL STAGES



Majority of the patients in clinical stage 1 had either mild or non significant immunodeficiency. 12.2% of the patients, though in clinical stage 1 (asymptomatic) had severe immunodeficiency.


IMMUNODEFICIENCY IN CLINICAL STAGE 2
45.00%
40.00%
35.00%
30.00%
25.00%
20.00%
15.00%
10.00%
5.00%
0.00%
38.46%
23.07%
15.38%
23.07%
NON SIGNIFICANT
MILD
ADVANCED
SEVERE
IMMUNODEFICIENCY

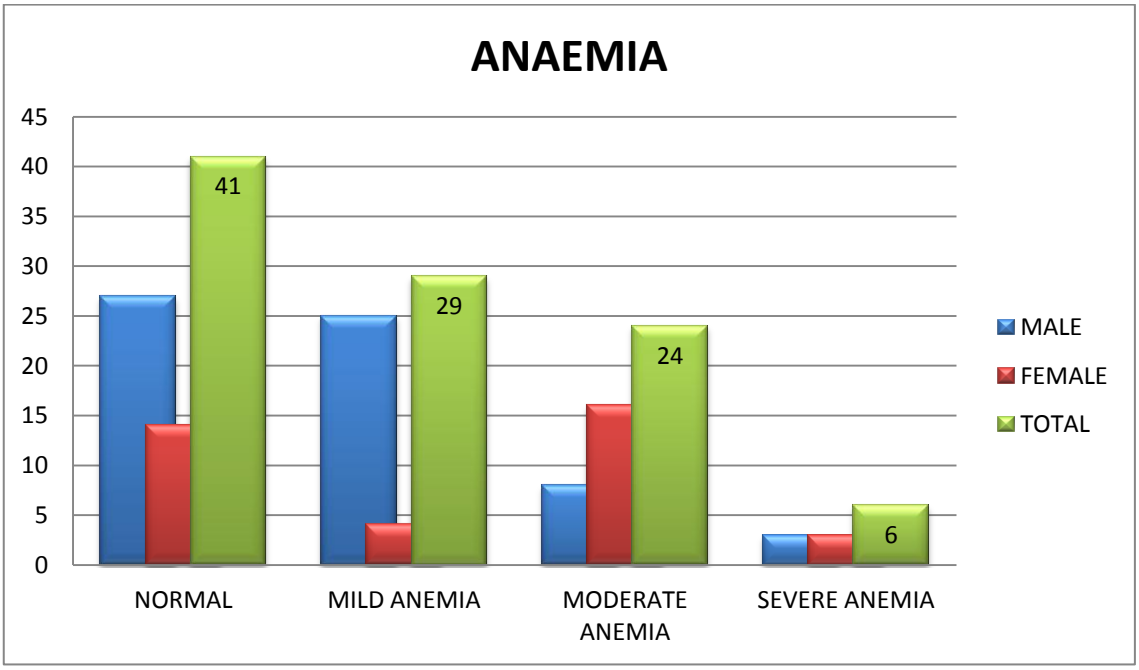

IMMUNODEFICIENCY IN CLINICAL STAGE 3
60.00%
50.00%
40.00%
30.00%
20.00%
10.00%
0.00%
6.98%
9.30%
32.55%
51.16%
NON SIGNIFICANT
MILD
ADVANCED
SEVERE
IMMUNODEFICIENCY



Moving from clinical stage 1 to clinical stage 4 there is an increase in patients in the advanced and severe immunodeficiency stage. The patients who had clinical stage 4 were all having severe immunodeficiency, suggesting a positive correlation between immunodeficiency based on CD4 count and clinical staging.

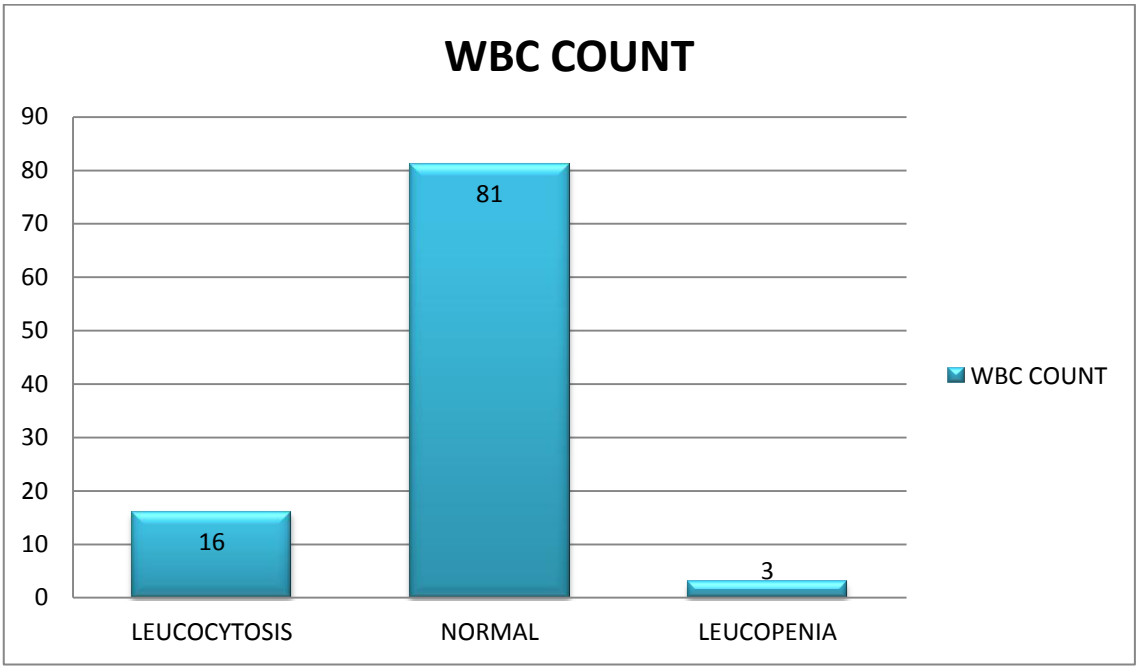
DISRTIBUTION OF ANEMIA BASED ON HEMOGLOBIN VALUES

RANGE	MALE	FEMALE	TOTAL
NORMAL	27	14	41
MILD ANEMIA	25	4	29
MODERATE	8	16	24
SEVERE	3	3	6



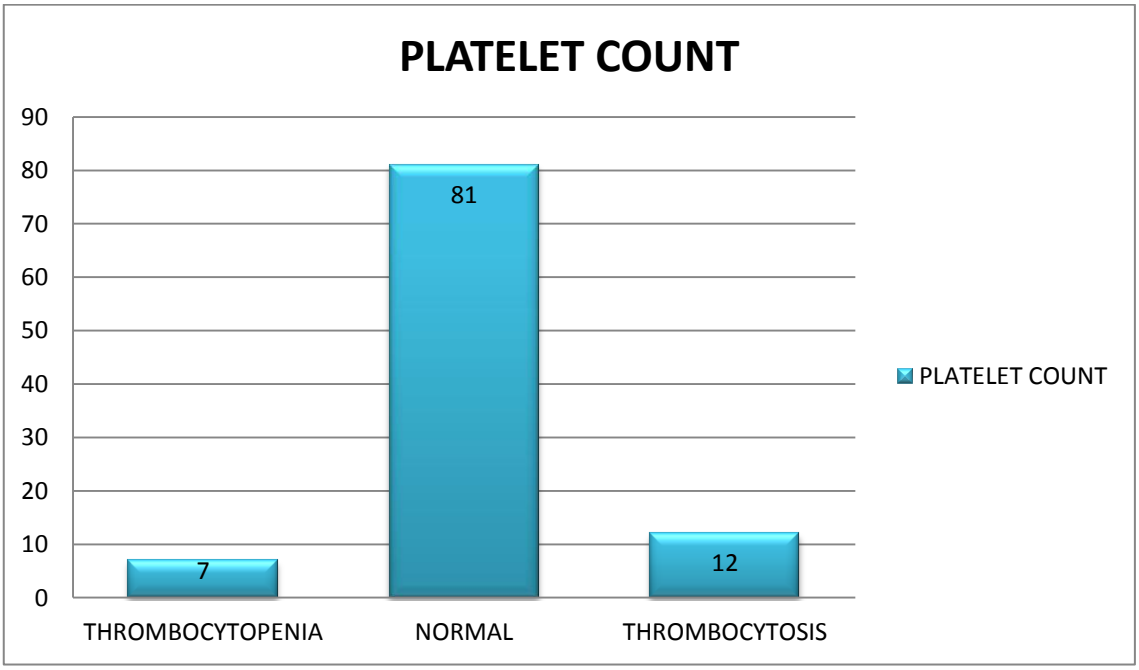
The prevalence of moderate to severe anaemia in study group was more in females compared to males. 51.35% of female patients had moderate to severe anaemia compared to 17.46 % of male patients.

DISTRIBUTION OF WBC COUNT



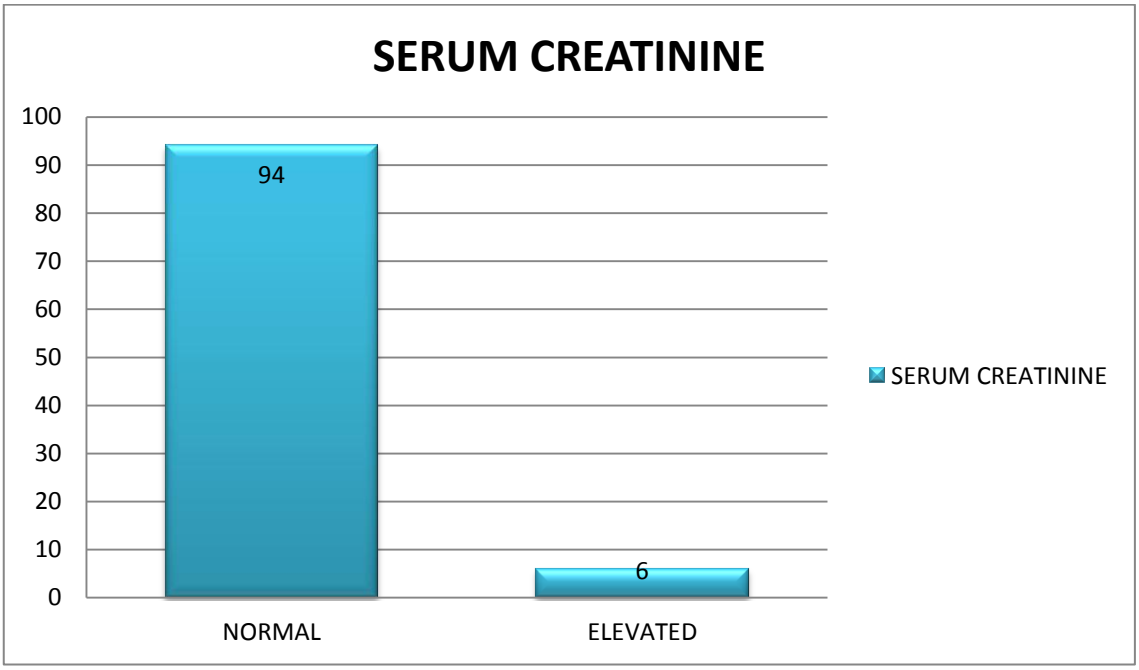
16% of the study population had leucocytosis and 3% had leucopenia.

DISTRIBUTION OF PLATELET COUNT



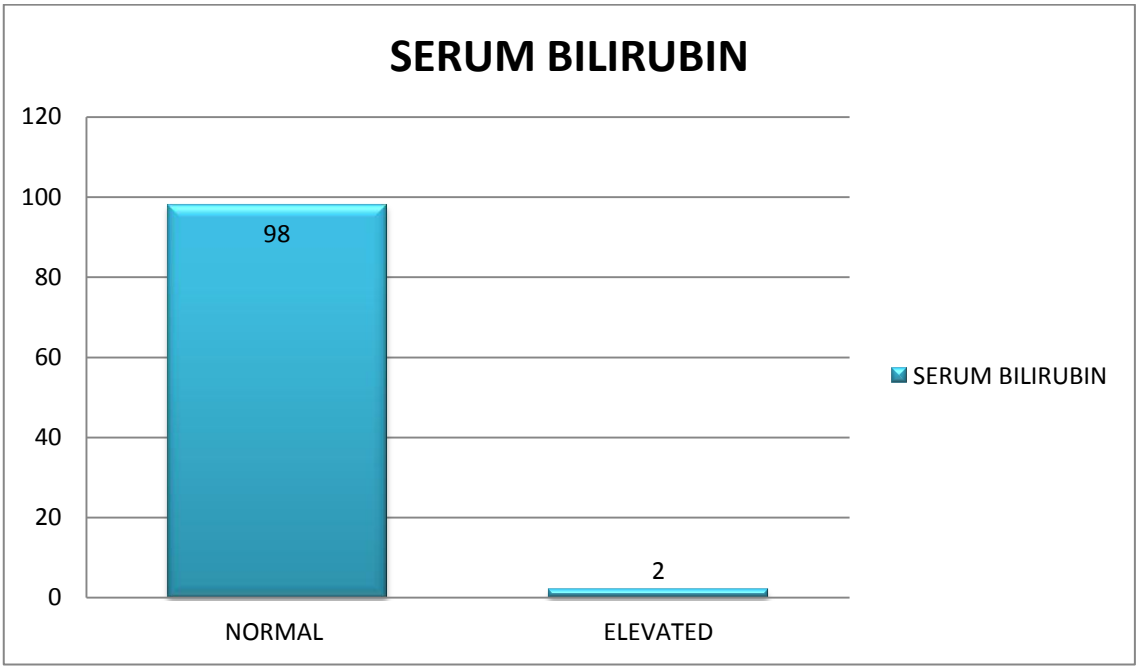
7% of the study population had thrombocytopenia.

DISTRIBUTION OF SERUM CREATININE LEVELS



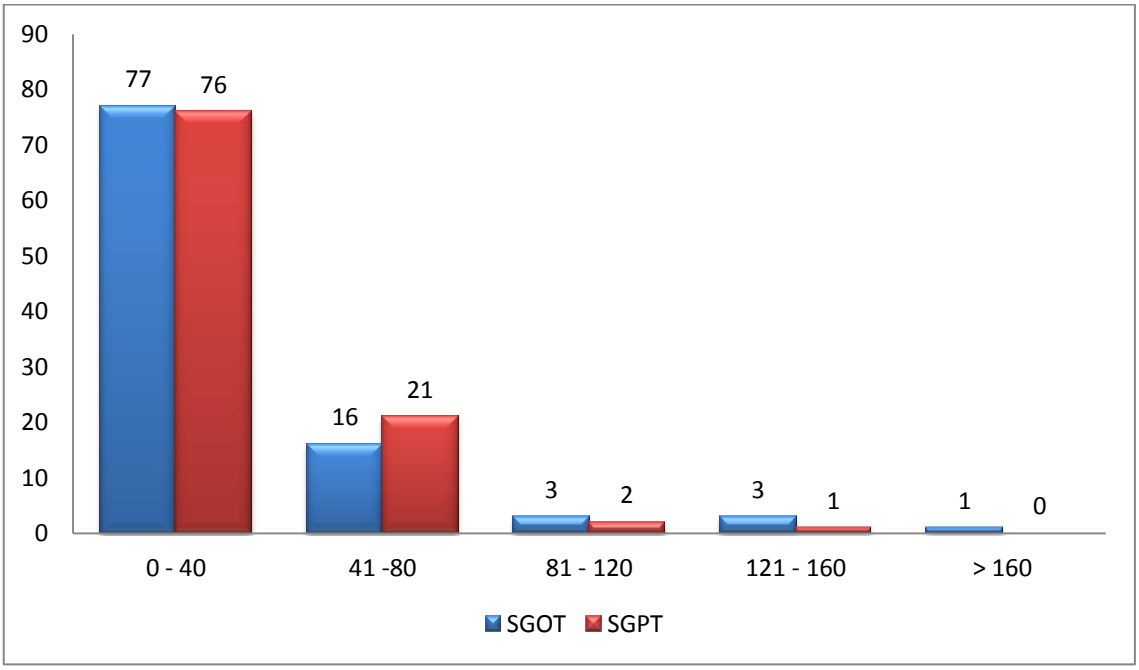
Serum creatinine was found to be elevated above normal limit in 6% of patients.

DISTRIBUTION OF SERUM BILIRUBIN LEVELS



Serum bilirubin was found to be above the normal range in 2% of the patients.

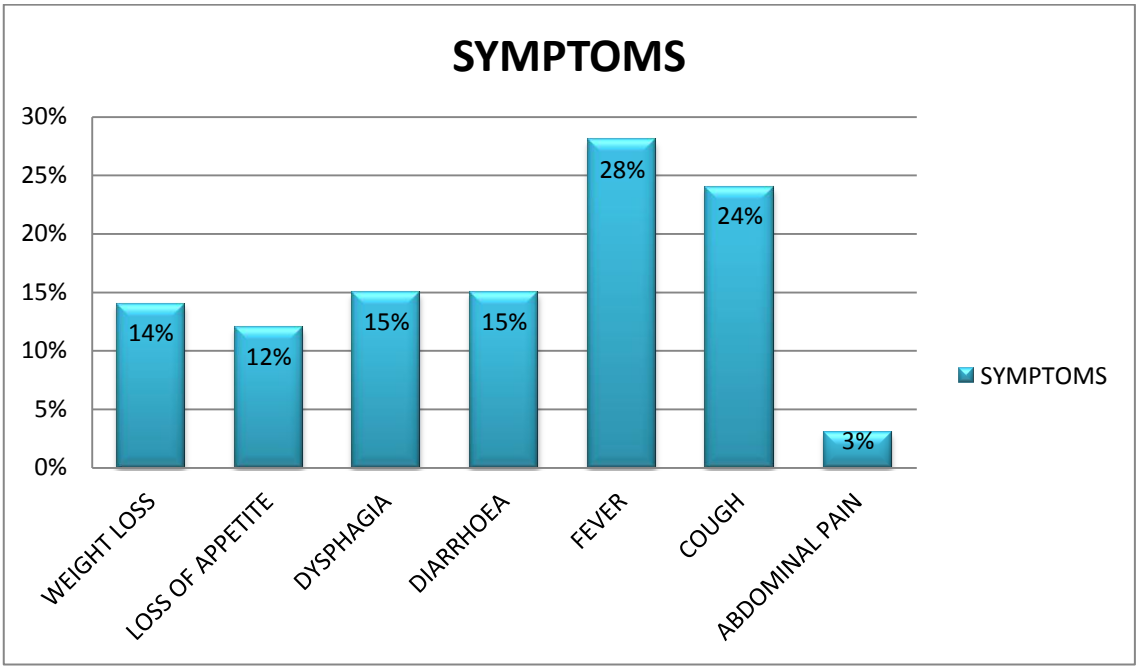
DISTRIBUTION OF SERUM TRANSAMINASES LEVELS (SGOT AND SGPT)



SGOT was found to be elevated in 23% of patients and it was above two times the upper limit of normal in 7% of patients.

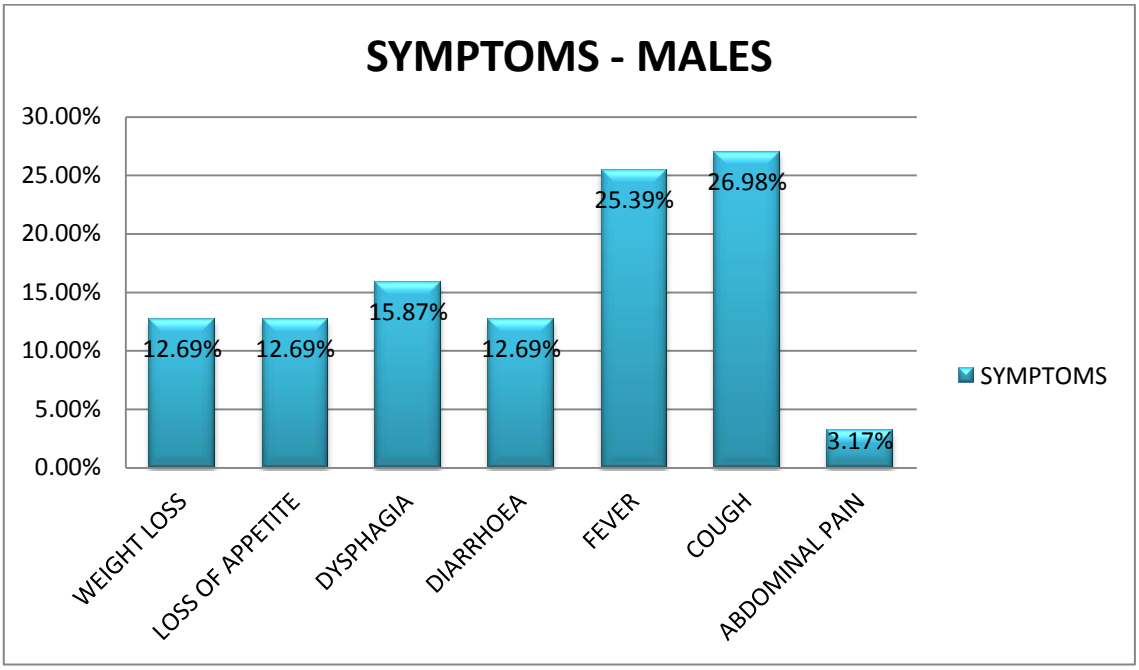
SGPT was found to be elevated in 24% of patients. It was above two times upper limit of normal in 3% of patients.

SYMPTOMATOLOGY

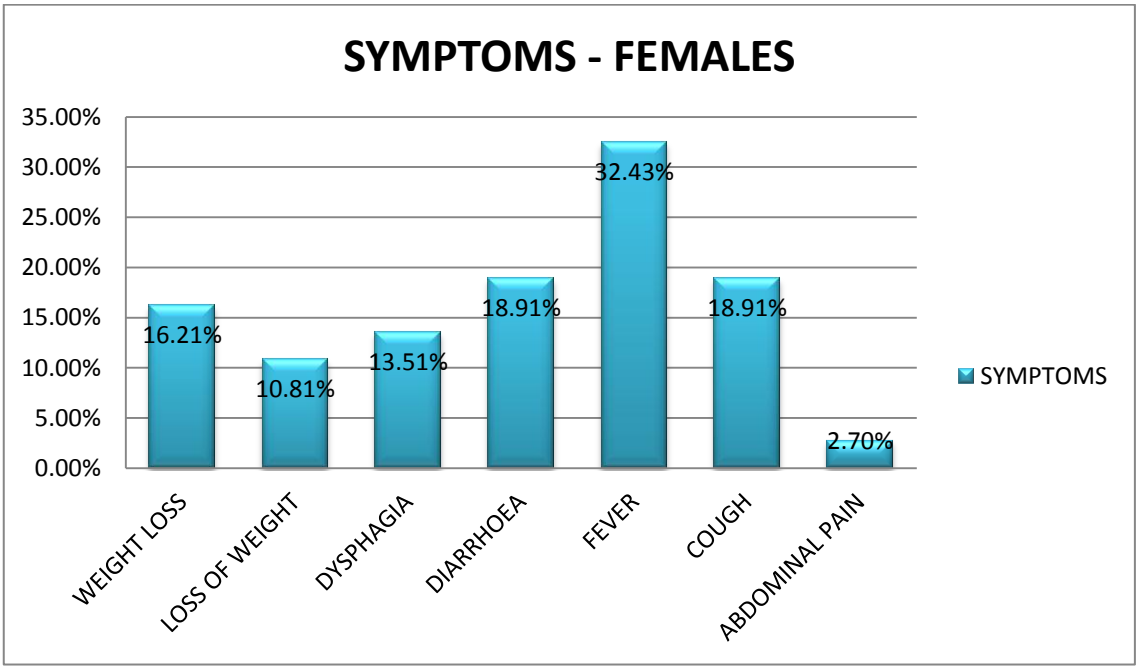


SYMPTOMS	MALE	FEMALE	TOTAL
WEIGHT LOSS	8	6	14
LOSS OF APPETITE	8	4	12
DYSPHAGIA	10	5	15
DIARRHOEA	8	7	15
FEVER	16	12	28
COUGH	17	7	24
ABDOMINAL PAIN	2	1	3

SYMPTOMATOLOGY – MALES



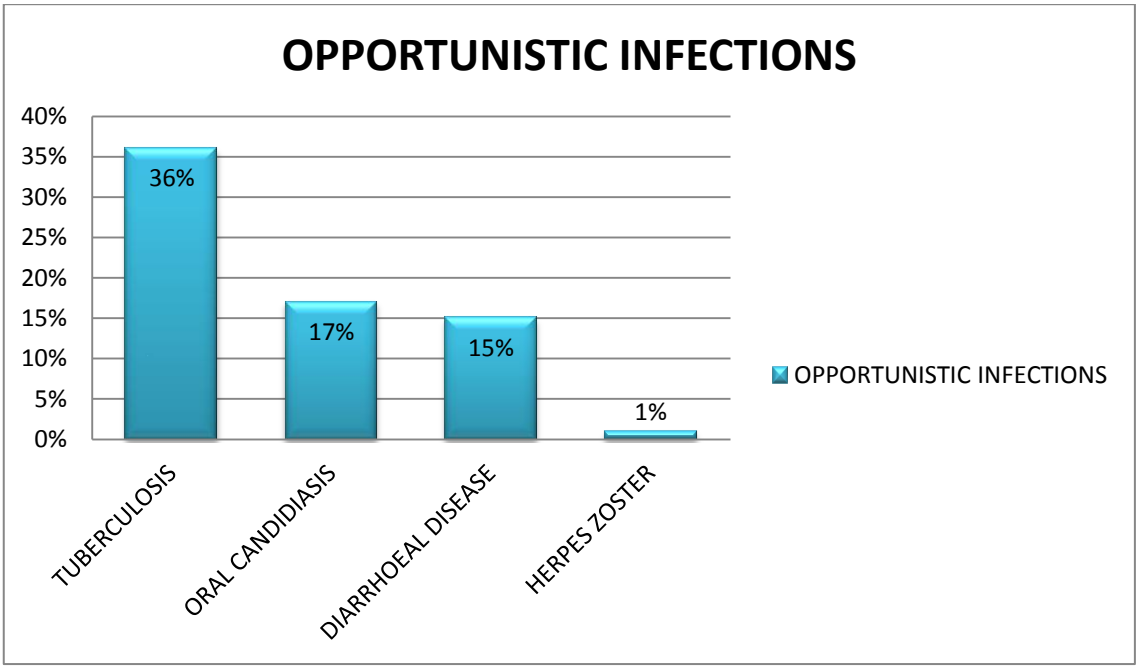
SYMPTOMATOLOGY – FEMALES



The most common symptom of the patients in the study population is fever (28%), followed by cough (24%), dysphagia (15%), diarrhoea (15%), eight loss (14%), loss of appetite (12%) and abdominal pain (3%).

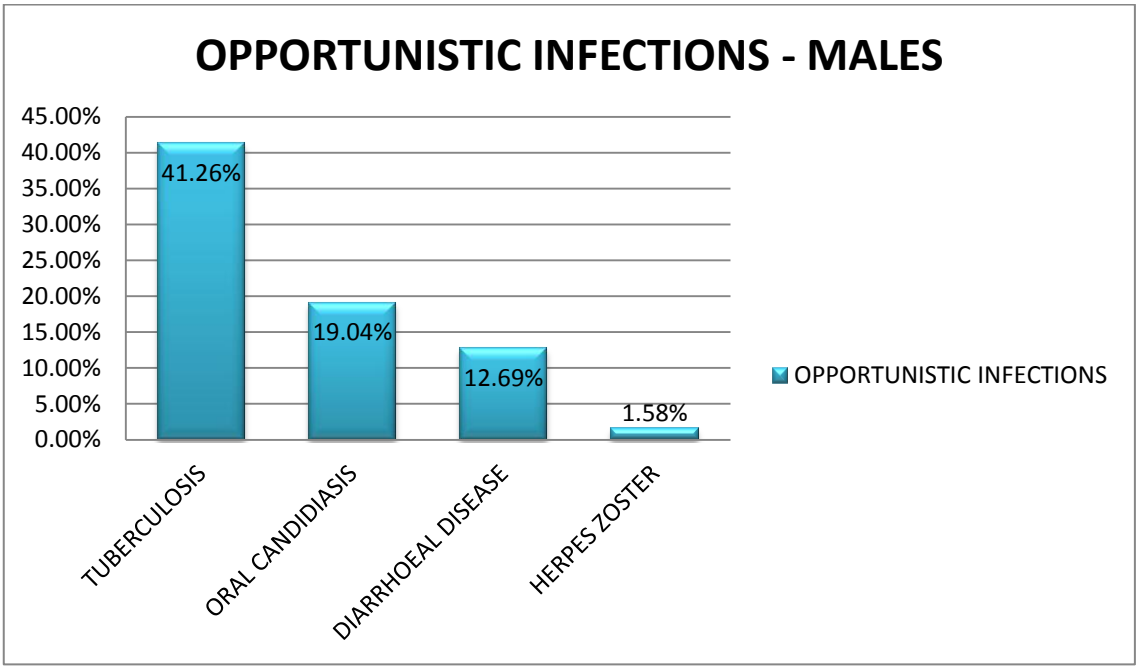
Cough (26.98%) was the predominant symptom among male patients, but the predominant symptom in the females was found to be Fever (32.43%).

OPPORTUNISTIC INFECTIONS – FREQUENCY DISTRIBUTION

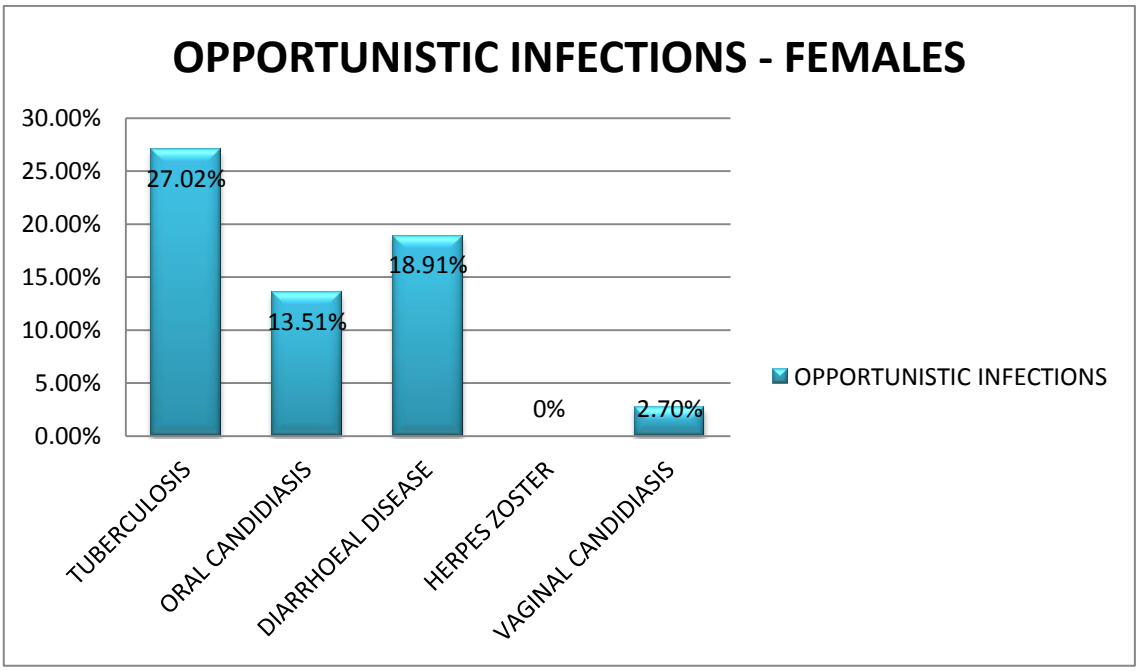


OPPORTUNISTIC INFECTIONS	MALE	FEMALE	TOTAL
TUBERCULOSIS	26	10	36
ORAL CANDIDIASIS	12	5	17
DIARRHOEAL DISEASE	8	7	15
HERPES ZOSTER	1	0	1
GENITAL CANDIDIASIS	-	1	1

OPPORTUNISTIC INFECTIONS IN MALES FREQUENCY DISTRIBUTION



OPPORTUNISTIC INFECTION IN FEMALES – FREQUENCY DISTRIBUTION



The commonest opportunistic infection related to HIV infection found in the study was Tuberculosis which was found in 36% of the study population. It was followed by Oral Candidiasis in 17% of patients and Diarrhoeal disease in 15% of the patients.

DISCUSSION

HIV/AIDS as already discussed has several clinical stages, variable pathogenesis and opportunistic infections. In this study, the clinical and laboratory profile of 100 patients, who were newly diagnosed were studied and documented. There were 63 male patients and 37 female patients in the study population. The majority of the newly diagnosed HIV patients belonged to the age group of 31 to 45 years, suggesting that the incidence and prevalence of the disease is more common in the sexually active period of life. 77% of the study population were literates and the rest were illiterates.

Body mass index distribution showed that 30% of the study population were under weight. Among them 21% were significantly underweight and 11% were severely wasted. These individuals may be part of HIV wasting syndrome. 37.8% of females were underweight compared to 25.3% of males.

WHO clinical staging and immunological classification were applied to the study population. 41% of the patients were in the clinical stage 1 and 43% in clinical stage 3. Higher number of patients in clinical stage 3 is because of the higher prevalence of Pulmonary Tuberculosis co-infection. Another factor is that in Tirunelveli medical college all patients diagnosed with tuberculosis are screened for HIV and, if they tested positive they fell into the category of clinical stage 3. It also illustrates the importance of

screening for HIV in patients with Tuberculosis and the vice versa. The clinical stage distribution showed a relatively similar trend in both males and females.

33% of the study population had severe immunodeficiency (based on WHO immunological classification for established HIV infection). 60% of the population had advanced immunodeficiency or more. When this immunological classification was applied to patients in individual clinical stage, there was a increase in patients with advanced or severe immunodeficiency when moving from clinical stage 1 to clinical stage 4 as expected. All the three patients who were in clinical stage 4 were found to be having severe immunodeficiency. Though various studies suggest that CD4 alone cannot be a true indicator of the immunodeficiency in a HIV infected patient, in this study there is a positive correlation between the immunodeficiency classification based on CD4 count and clinical stage of the disease.

The prevalence of moderate to severe anaemia in the study population was 30%. 51.35% of females had moderate to severe anaemia compared to 17.46% in males. Hence there is increased prevalence of anemia in the female HIV infected patients, when compared to males. This may be explained by the fact that anemia is more prevalent in females than in males in this locality.

16% of the study population had leucocytosis and 3% had leucopenia.7% of the study population had thrombocytopenia. It is also important to note that unexplained anaemia (<8 g/dl), neutropenia (<0.5 × 109 per litre) or chronic thrombocytopenia (<50 × 109 per litre), in a HIV infected patient is classified as clinical stage 3 according to WHO. So the cause of such haematological problems in a HIV infected patient should be investigated.

Serum creatinine was found to be elevated in 6% of patients. The presence of increased serum creatinine in a HIV positive patient may be due to either HIV itself (HIV associated nephropathy) or may be due to antiretroviral drugs. This study was conducted in HAART naïve patients, so there is no possibility of anti retroviral drugs induced renal failure in this study group. Also HIV infected individuals are more prone to prerenal azotemia due to volume depletion occurring from salt wasting, poor nutrition, nausea and vomiting. To find out the presence of HIV associated nephropathy additional investigations should be done like 24 hours urine protein to demonstrate nephrotic range of proteinuria and renal biopsy to prove the presence of focal segmental glomerulosclerosis.

Serum bilirubin was found to be elevated in 2% of the patients. Liver transaminase enzymes were elevated in 24% of patients. However SGOT and SGPT was elevated two times upper limit of normal only in 7% and

3% respectively. Such abnormality in HIV infected patients prompts the screening for hepatitis B or C co-infection in them. Many of the patients in this study who were found to be HIV infected were already taking anti tuberculous therapy for Tuberculosis. Elevated serum bilirubin and transaminase levels above 2 times upper limit of normal in such patients may be due to drug induced liver injury. Those with only transaminase elevation less than 2 times the upper limit of normal may be due to liver adaptation to anti tuberculous therapy.

The most common symptom in the study population was fever (28%), followed by cough(24%). Cough was the most common symptom in male patients, while in females fever was the most common symptom. Patel AK et al and Kothari K et al in their respective studies had already found fever as the commonest symptom. This proved to be true in this study also.

The commonest opportunistic infection in study population was pulmonary tuberculosis in 36% of the patients. It was followed by oral candidiasis (17%) and diarrhoeal disease (15%). According to Patel AK et al, the most common opportunistic infection was oral candidiasis followed by tuberculosis. Studies conducted by Vajpayee et al and Zaheer et al had shown that tuberculosis is the commonest opportunistic infection. Tuberculosis as the most common opportunistic infection in this study can be attributed to the high prevalence of tuberculosis in this locality.

CONCLUSION

Most of the newly diagnosed HIV infected patients belong to the age group of 31 to 45 years of age. There is a positive correlation between the clinical stage and the immunodeficiency based on CD4 count. Fever is the most common symptom in newly diagnosed HIV infected patients, followed by cough. Tuberculosis is the most common opportunistic infection followed by oral candidiasis. All patients with HIV infection should be screened for Tuberculosis and vice versa.

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16) Clinical Profile of HIV/AIDS-infected Patients Admitted to a New Specialist Unit in Dhaka, Bangladesh—A Low-prevalence Country for HIV Nashaba Matin, Lubaba Shahrin, Mohammed Moshtaq Pervez, Sayera Banu, Dilruba Ahmed, Mahmuda Khatun, and Mark Pietroni

17) Clinical Profile of HIV/Aids Patients in Srinagar, Kashmir, India Kaiser Ahmed Wani

18) Clinico-epidemiological profile of HIV patients attending ART centre in rural Western Maharashtra, India

Jayant D. Deshpande1, Purushottam A. Giri2, Deepak B Phalke3

ANNEXURES

ANNEXURE 1

WHO CLINICAL STAGING FOR HIV IN ADULTS

Clinical stage 1
Asymptomatic Persistent generalized lymphadenopathy
Clinical stage 2
Moderate unexplained weight loss (<10% of presumed or measured body weight)[i] Recurrent respiratory tract infections sinusitis, tonsillitis, otitis media and pharyngitis) Herpes zoster Angular cheilitis Recurrent oral ulceration Papular pruritic eruptions Seborrhoeic dermatitis Fungal nail infections

Clinical stage 3
Unexplained[i] severe weight loss (>10% of presumed or measured body weight) Unexplained chronic diarrhoea for longer than one month Unexplained persistent fever (above 37.6°C intermittent or constant, for longer than one month) Persistent oral candidiasis Oral hairy leukoplakia Pulmonary tuberculosis (current) Severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis or bacteraemia) Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis Unexplained anaemia (<8 g/dl), neutropaenia (<0.5 × 10^9 per litre) or chronic thrombocytopaenia (<50 × 10^9 per litre)

Clinical stage 4[ii]
HIV wasting syndrome
Pneumocystis pneumonia
Recurrent severe bacterial pneumonia
Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month's duration or visceral at any site)
Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
Extrapulmonary tuberculosis
Kaposi's sarcoma
Cytomegalovirus infection (retinitis or infection of other organs)
Central nervous system toxoplasmosis
HIV encephalopathy
Extrapulmonary cryptococcosis including meningitis
Disseminated non-tuberculous mycobacterial infection
Progressive multifocal leukoencephalopathy
Chronic cryptosporidiosis (with diarrhoed)
Chronic isosporiasis
Disseminated mycosis (coccidiomycosis or histoplasmosis)
Recurrent non-typhoidal Salmonella bacteraemia
Lymphoma (cerebral or B-cell non-Hodgkin) or other solid HIV-associated tumours
Invasive cervical carcinoma
Atypical disseminated leishmaniasis
Symptomatic HIV-associated nephropathy or symptomatic HIV-associated cardiomyopathy

ANNEXURE 2

WHO IMMUNOLOGICAL CLASSIFICATION FOR

ESTABLISHED HIV INFECTION

HIV-associated immunodeficiency	Age-related CD4 values			
	<11 months (%CD4+)	12–35 months (%CD4+)	36–59 months (%CD4+)	>5 years (absolute number per mm³ or %CD4+)
None or not significant	>35	>30	>25	> 500
Mild	30–35	25–30	20–25	350–499
Advanced	25–29	20–24	15–19	200–349
Severe	<25	<20	<15	<200 *or* <15%

ANNEXURE 3

PROFORMA

Patient Name: **Age**

Address **ART No**

Height:

Weight:

Symptoms:

Clinical Findings

Comorbidities

CD4 Count:

CLINICAL STAGE:

Hb		
TC		
DC		
ESR		
Platelets		

RBS	**Urea/ Creatinine**

Sodium :

Potassium:

Liver Function Test :

ANNEXURE 4 - MASTER CHART

patient name	age	sex	ART no	literacy	BMI	Clinical stage	CD4	TC	HB%	platelet	SGOT	SGPT	bilirubin	creatinine	urea
muppidathi	46	male	6752	yes	25.8	3	131	4600	11.1	4.77	35	44	0.8	1	37
sivasangu	64	male	6754	no	18.81	2	336	8100	12.6	1.83	24	15	0.6	1.3	32
madasamy	43	male	6756	yes	24.31	1	448	9000	16.8	4.83	17	45	0.8	0.8	30
thennarasu	30	male	6757	yes	22.65	1	475	11,700	14.7	3.77	18	53	0.8	0.8	20
velsamy	30	male	6759	yes	16.52	1	420	5800	12	4.21	40	39	0.9	0.9	32
indira	45	female	6760	no	15.86	3	37	2000	6.7	1.99	18	23	0.7	0.7	16
masanam	33	male	6761	yes	18.36	1	206	8000	15	2.55	20	45	0.7	0.7	18
kasiham	37	female	6765	no	25.07	1	480	6100	12.1	3.01	15	21	0.6	0.7	28
meena	16	female	6766	no	20	1	233	8400	12.1	2.33	47	39	0.6	0.6	19
baskar	32	male	6768	yes	18.59	3	256	6700	14.6	3.79	26	43	0.5	0.7	19
ganesan	35	male	6770	yes	19.53	3	31	12200	7.9	1.7	26	35	4.2	0.7	30
kaliammal	40	female	6772	no	14.8	3	393	8000	10.9	3.83	30	42	0.6	1.4	64
pandiyaraj	38	male	7004	yes	18.72	3	252	2500	12.3	2.23	92	79	0.6	0.8	18
sundarraj	39	male	7005	yes	22.22	2	28	4300	12.3	2.7	37	42	0.6	1	25
joeswa	40	male	7006	yes	13.76	3	32	6300	8.9	4.88	28	20	0.7	0.8	18
athina	25	female	7007	yes	30.61	1	182	6000	12.8	4.13	18	16	0.4	0.8	18
gopal	38	male	7008	no	19.07	3	253	9500	8.4	2.98	16	12	0.5	0.9	20
gomathy	33	female	7009	no	16.84	3	384	5800	11.8	1.82	28	26	0.8	0.9	30
sudalaimani	23	male	7010	yes	24.31	1	713	6200	12.3	1.91	28	26	0.6	1	24
velkumar mariappan	32	male	7012	yes	22.14	1	361	8800	12.4	4.01	20	20	0.8	1.2	19
sathiya rani	27	female	7013	yes	20.82	1	679	7000	13	4.21	22	15	0.9	0.9	16
ananda kumar	37	male	7019	yes	23.5	1	283	9900	15.9	5.01	30	36	0.5	1	16
palani	41	male	7021	yes	18.26	2	287	6900	11.1	3.86	23	20	0.6	0.7	19
sudalee	39	female	7023	yes	19.7	2	437	5600	13.7	3.34	15	13	0.5	1	16
mangalaraj	57	male	7024	yes	19.72	3	60	7500	10.4	3.21	45	52	1.4	1	30
manimaran	21	male	7042	yes	18.73	1	631	12,800	15.6	4.88	23	29	0.5	0.9	18
ananth	20	male	7043	yes	15.35	1	81	6800	11	4.11	18	20	0.4	0.8	16
abdul hameedu	60	male	7044	no	20.96	4	50	4700	14.2	5.34	25	16	0.8	1	16
manikandan	30	male	7046	yes	20.93	3	479	1900	13.8	3.12	38	29	0.8	0.8	18
samy	41	male	7045	yes	21.3	2	33	5500	11.3	2.13	22	25	0.6	0.8	30
mallika	29	female	7047	yes	22.63	2	662	8000	12.3	4.49	37	25	0.8	0.7	19
anandh	40	male	7048	yes	21.08	3	596	8800	11	1.83	24	27	0.4	0.6	30
paramasivan	46	male	7049	no	22.31	3	239	5700	14.4	5.08	16	14	0.7	0.8	18
mohamed ajesh	44	male	7145	yes	18.73	2	802	4700	11.7	1.2	25	18	1	1	20
rosammal	40	female	7146	yes	22.67	3	172	4100	11.3	1.78	28	23	0.5	0.9	16
shanmugavel	48	male	7147	no	17.12	3	56	4900	12.9	2.21	57	39	0.6	1	18
murugan	52	male	7150	yes	15.56	3	206	5600	10.1	3.44	32	11	0.7	0.8	16
poomari	28	female	7051	yes	16.2	2	420	11,700	8.9	1.4	129	80	0.7	0.8	30
rajesh	37	male	7052	yes	24.21	1	404	6200	15.1	1.4	54	50	1.5	0.8	17
nainar murugan	33	male	7053	yes	20.68	1	272	5700	13.6	2.1	43	40	0.5	1	16
navaneethakrishnan	24	male	7054	yes	20.45	1	122	6300	11	1.85	32	22	0.8	0.8	24
anthony	54	male	7055	no	20.2	3	146	6200	11.6	2.33	25	15	0.6	1	18
manikandan	20	male	7056	yes	15.27	2	1198	8000	10.5	2.18	32	34	0.8	0.9	16
shanmugapriya	18	female	7057	yes	19.56	1	842	7200	8.5	1.2	43	51	0.9	0.8	20
manonmani	47	female	7058	no	16.87	3	221	4300	6.1	1.5	109	100	0.9	0.8	19
sundar nadar	50	male	7059	yes	21.5	3	156	8000	10.9	1.81	27	16	0.8	0.8	20
mydeen meeral	45	female	7060	no	16.01	4	93	6300	12.4	1.75	130	50	1	1	22
nadarajan	50	male	7263	yes	26.03	1	207	5000	12.9	2.95	27	23	0.6	1	23
madathi	55	female	7264	no	26.16	2	404	5700	11.9	3.15	20	25	0.6	1	37
mariammal	36	female	7265	yes	15.3	3	35	7500	8.5	3.57	150	172	0.4	0.7	23
velukonar	60	male	7266	yes	18.75	3	526	8600	11.6	3.66	35	12	0.4	1.2	27
arumugam	35	male	7267	yes	19.53	1	259	9800	9.6	3.13	26	32	0.4	1	21
sakthi	34	male	7268	yes	19.53	4	98	6600	13.1	3.75	62	80	1.2	0.8	39
selvi	35	female	7270	yes	15.97	3	53	7000	10.8	2.78	59	70	0.6	0.8	20
kumar	33	male	7271	yes	16	3	295	7200	14	1.84	32	34	0.9	0.8	32
muthukumar	29	male	7273	yes	18.8	1	600	5900	13.7	1.64	172	88	0.8	0.6	16
regina	45	female	7274	no	16.88	3	250	3900	7.9	1.82	17	11	0.4	0.7	18
ganesan	41	male	7275	yes	21.67	1	267	8300	12.5	2.8	40	38	0.6	0.9	20
iyappan	56	male	7276	yes	16.16	3	114	4400	7.5	2.95	31	23	0.5	0.8	16
kanimozhi	26	female	7277	yes	20.93	1	330	3500	10.4	2.06	103	76	0.4	0.7	19
rajeshwaran	55	male	7278	yes	21.33	3	33	10,400	8.9	4.47	38	54	0.4	0.6	19
saravanan	43	male	7279	yes	17.25	1	321	9500	9.3	3.45	32	23	0.4	0.9	28
muthumari	39	female	7280	yes	14.2	3	131	6000	9.9	3.6	48	35	0.4	0.6	16
shanthi	40	female	7281	yes	21.33	1	588	8200	15	2.3	40	38	0.8	0.1	40
sudha	40	female	7282	yes	17.36	3	122	7900	9	3	18	34	0.4	0.6	18
saroja	30	female	7283	no	18.33	2	992	6500	13.4	3.2	18	18	0.4	0.7	26
suganya	27	female	7284	yes	21.4	1	626	6200	12.5	3.11	20	27	0.6	0.6	17
paul durai	40	male	7285	no	25.8	2	501	7200	14	2.38	42	46	0.5	1	18
mathakani	55	female	7286	yes	14.76	3	201	10,300	8	2.29	34	44	0.4	0.7	16
mariappan	40	male	7287	yes	26.91	1	237	8600	14.4	2.89	48	17	0.6	0.7	16
sekar	46	male	7288	yes	18.02	3	295	6300	17.1	1.85	22	20	0.7	0.7	22
senthil	25	male	7289	yes	30.86	1	665	9100	15	1.91	27	10	1	0.7	23
helen	35	female	7290	yes	23.23	2	39	4800	13.1	2.1	46	28	0.6	0.7	22
manickam	28	male	7292	yes	23.44	3	305	4800	11.9	3.2	33	53	0.5	0.9	16
murugan	60	male	7293	yes	20.31	3	167	12000	14	1.25	40	36	0.8	1.1	40
rajagopal	40	male	7300	yes	17.09	3	42	6300	11.1	4.82	181	84	0.4	0.7	16
karupayee	54	female	7299	no	24.77	1	1141	11600	11.7	2.53	41	26	0.4	1.6	48
esakimuthu	45	male	7298	yes	16.59	3	67	6500	11.4	1.69	30	39	0.6	0.9	20
parvathy	37	female	7297	yes	25.45	1	866	5800	13	1.82	40	36	0.8	0.9	31
manoharan	38	male	7296	yes	28.57	1	240	6200	14.5	2.69	32	24	0.7	0.9	16
bindhu	26	female	7295	yes	19.53	1	368	5800	14	2.12	45	36	0.7	0.9	32
revathi	29	female	7294	yes	27.33	1	647	10100	10	2.14	21	12	0.5	0.6	18
ponraj	40	male	7339	yes	31.25	1	535	8100	16	2.62	37	22	0.7	0.8	20
arumugam	31	male	7342	yes	16	3	282	10300	13	2.57	23	13	0.4	0.8	16
murugan	50	male	7340	yes	25.29	1	351	6100	15.3	2.9	18	21	0.8	1	30
chelladurai	35	male	7357	yes	20.4	3	192	10100	13	2.87	17	16	0.6	0.7	31
jeyaraman	50	male	7336	yes	21.64	3	48	5300	11.9	2.18	30	26	0.4	0.6	15
rajesh	18	male	7348	yes	18.08	1	196	6600	15	1.98	38	30	1	1.3	23
surya rani	49	female	7338	yes	18.51	3	303	5500	10.9	2.1	40	15	0.4	0.7	18
sudalaimuthu	65	male	7350	no	23.87	3	470	5300	11.2	1.98	20	12	0.4	1.1	24
sudalaimuthu	36	male	7349	no	20.44	1	358	7500	14.6	3.33	30	12	0.7	0.8	16
mary	48	female	7347	yes	22.71	1	176	8900	9.2	3.47	31	25	0.3	0.9	15
anand	42	male	7346	yes	31.24	1	785	7500	12.5	3.04	24	19	0.6	0.7	16
mani rose mary	33	female	7345	yes	22.34	3	144	6900	10.3	3.03	39	14	0.4	0.7	18
nagarajan	50	male	7344	no	30.67	3	539	7344	16.6	1.67	41	17	0.9	0.8	19
roja	27	female	7343	yes	26.82	1	200	9500	13.2	3.7	30	15	0.8	0.8	16
vadivu	41	female	7341	yes	28.98	3	158	4000	11.8	2.51	18	10	0.4	0.6	16
raju	38	male	7355	yes	19.9	1	456	6700	12	3.33	28	29	0.6	0.7	18
esakimuthu	41	female	7356	no	16.67	1	550	9800	13	2.01	40	44	0.8	0.8	16
mariammal	44	female	7262	no	20.7	1	436	5500	10.3	3.05	28	30	0.7	1	36